

# CLINICAL TUBERCULOSIS

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## PREFACE TO FOURTH EDITION

It is gratifying to have reached four editions of *Clinical Tuberculosis* before ten years have passed. There is very little doubt but that a better appreciation exists today in medical practice of tuberculosis pathology. This appreciation, particularly, is noted in a better understanding of the sensitivity reaction phenomena which produces pathological types of this disease, not always evident at the postmortem table. Thus, a newer understanding of the management of benign pulmonary exudative tuberculous phenomena has been developed. This edition has allowed the bringing up to date of statistical data accumulated in World War II, which emphasizes the alterations made necessary as a result of adjustments in life in war. Chemotherapy in tuberculosis is coming to the forefront with the development of the Sulfonamides and Sulfones, and it is apparent that there should be, very shortly, a chemical which might satisfactorily destroy the tubercle bacillus in the human as well as in the animal. This work we have reviewed to date. It might not be amiss to point out once more the important place of roentgen studies in this disease. Therefore, the two hundred and sixty x-ray illustrations make a veritable atlas for such study in this book.

I again thank the publishers for their fine cooperation, and also my very dear friend, Godias J. Drolet, who is so painstaking in his accumulation of statistical data and the charting thereof, all of which is so important to us in this work.

BENJAMIN GOLDBERG.

58 E. Washington St., Chicago, Ill.

## PREFACE TO FIRST EDITION

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**T**HIS work presents in correlated form the entire subject of Clinical Tuberculosis. Encyclopedic in scope, the unity of the text material is definitely enhanced by the inclusion of chapters by specialists in every branch of medicine and surgery.

No one will dispute the fact that tuberculosis still ranks as one of the outstanding scourges of civilized peoples. It will doubtless continue as such until, at least, the time when a specific remedy for the disease is discovered. Until then the present plan of management, which includes all the newer advances in surgical therapy, stands out as our most powerful weapon of attack. This holds true for extra-pulmonary, as well as for the pulmonary disease.

In years past institutions specializing in the treatment of the tuberculous patient were far removed from medical centers. This situation was a decided disadvantage, as it deprived afflicted individuals of the benefits of systematic diagnosis and therapy. While the tuberculous involvement itself received adequate supervision, there was lacking a system which embraced a thorough study of all possible coexisting affections.

The modern tuberculosis sanatorium has largely overcome this deficiency by development of the general hospital plan. Such a plan provides every facility for a diagnosis and therapy and, while the tuberculous lesion is the main objective, every condition which might influence it unfavorably is seriously considered.

This augmented status of present day management has contributed to an enlightened comprehension of clinical tuberculosis—a comprehension which every practitioner of medicine, be he specialist in one field or another, can gather from the chapters which follow.

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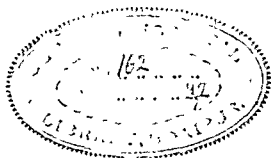
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**SECTION A.**

**(Chapters I to V.)**

**Epidemiology, Bacteriology, Immunology,  
Histopathology, and Pathologic  
Physiology.**

## CHAPTER I.

# EPIDEMIOLOGY OF TUBERCULOSIS.\*

GODIAS J. DROLET.

**Historical.**—The epidemic character of tuberculosis is undoubted, though in contrast with the more acute infections it manifests itself in comparatively slow-moving cycles, sometimes through several generations or across a series of communities. But it still follows the same general course: widespread at times; common to particular localities or among certain groups; moves wave-like with definite rises when it comes across virgin soil and gradually declines as resistance is evolved; finally, it may flare up again where contact has been lost.

The absence of national or accurate vital statistics until comparatively recent times makes difficult measured statements of the presence or ravages of tuberculosis though individual instances of the disease extend as far back as the Egyptian mummies themselves.

According to Brownlee,<sup>1</sup> in London, in 1655, "phthisis" was responsible for more than 20 per cent of all the deaths; in 1715, the proportion was lower, 13 per cent; but, it rose steadily until 1801 when it caused 30 per cent of all mortality; on the other hand, in 1939, tuberculosis had declined to 6 per cent of the deaths. Brownlee adds, "... the epidemic of phthisis in London is coming to an end, the course of which apparently has been something like two hundred years."

Dowling,<sup>2</sup> City Inspector of New York, with access to mortality records extending as far back as 1804, shows that in that year, in a grand total of 2125 deaths from all causes, 492 or 23 per cent were due to "consumption." Nowadays, deaths from pulmonary tuberculosis in New York City are only 4 per cent of all deaths—even while mortality previously heavy from many communicable diseases like diphtheria and typhoid or "summer complaints" among infants that formerly swelled the total has been brought under control.

One hundred and thirty years' record of pulmonary tuberculosis in three large American cities, New York City, Philadelphia and Boston, has been put together

---

\*In the summary treatment of such a broad subject as the Epidemiology of Tuberculosis, where the mere spread of data available as to the historical aspects of the disease at various times could make up a volume, the writer has felt it would be more useful here, first, to reduce theorizing or expressing opinions and, secondly, to present as succinctly as possible either in graphic or tabular form the latest, reliable data so as to furnish the competent reader a definite basis to form correct judgments. Furthermore it has been assumed that since this volume is primarily by American authors that manifestations of tuberculosis particularly in the United States could best be presented and would be of more immediate interest.

Broad use has been made of the Mortality Statistics of the United States Bureau of the Census and of the Epidemiological Reports of the Health Section of the League of Nations. Special acknowledgments are due the statistical service of the National Tuberculosis Association, which very kindly made available unpublished, up-to-date data, and to Mrs. Rosalie D. Hart for valuable assistance.

by Hoffman for the period 1812 to 1912, and by the writer subsequently for another quarter of a century (see Fig. 1). From 1812 until the 1840's the death rate, in the combined population of these three American centers, maintained

### PULMONARY TUBERCULOSIS DEATH RATE SINCE 1812 IN NEW YORK,\* PHILADELPHIA AND BOSTON

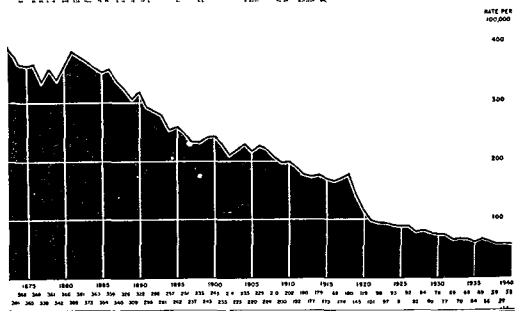
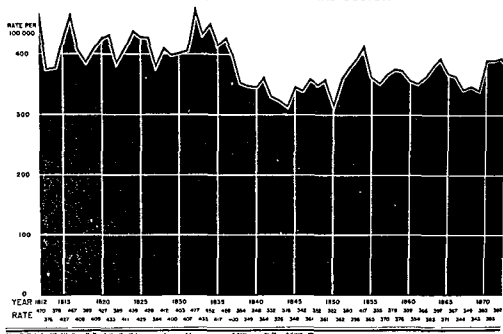


Fig. 1.

Note Between 1812 and 1940 incl the deaths in the 3 cities totaled 734,476 \*Manhattan and Bronx boroughs only. Original data compiled by the Prudential Insurance Company of America for period 1812 to 1912, thereafter by Research Service, New York Tuberculosis and Health Association, Inc.

itself steadily around or slightly above 400 per each 100,000; then, after a drop for a comparatively short period, it settled at a level around or above 300 until the 1880's, when it definitely broke into an almost continuous decline down to 58.

# EVOLUTION OF TUBERCULOSIS MORTALITY IN CERTAIN EUROPEAN COUNTRIES AS RECORDED IN BELGIUM, ENGLAND AND WALES, IRELAND, SCOTLAND, THE NETHERLANDS AND DENMARK

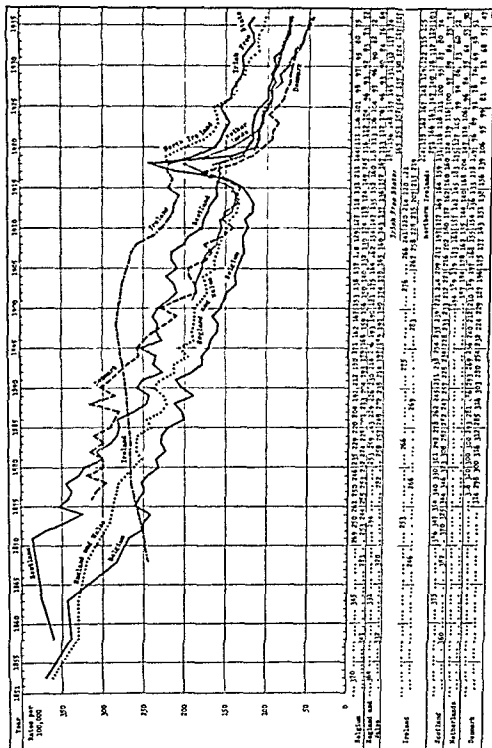


Fig. 2.

From Epidemiological Reports, Health Section, League of Nations.  
Charted by G. J. Drolet, New York Tuberculosis and Health Association.

Instances where the tuberculosis wave is known to have reached a crest in comparatively recent times are Sweden in the 1830's and, at comparatively still more recent dates, Australia, 1885; Bavaria, 1888-90; Ireland, 1898; Norway, at the close of the nineteenth century; Hungary, 1903; Uruguay, 1916; Japan, 1918. (Higher peaks occurred in certain places during World War I or the

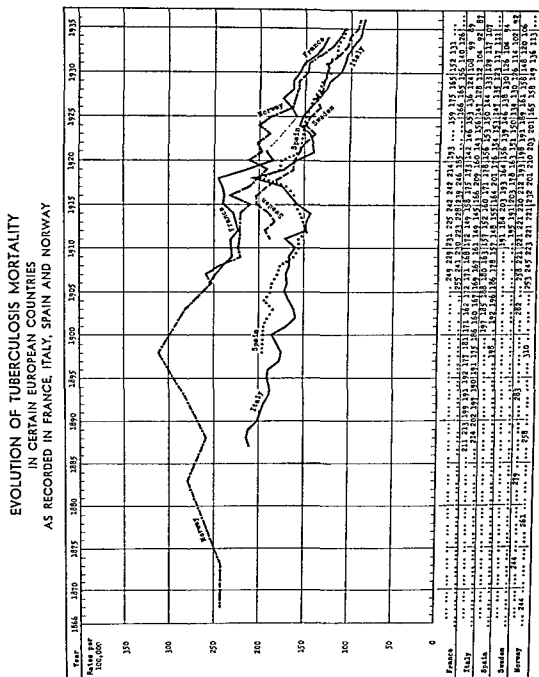
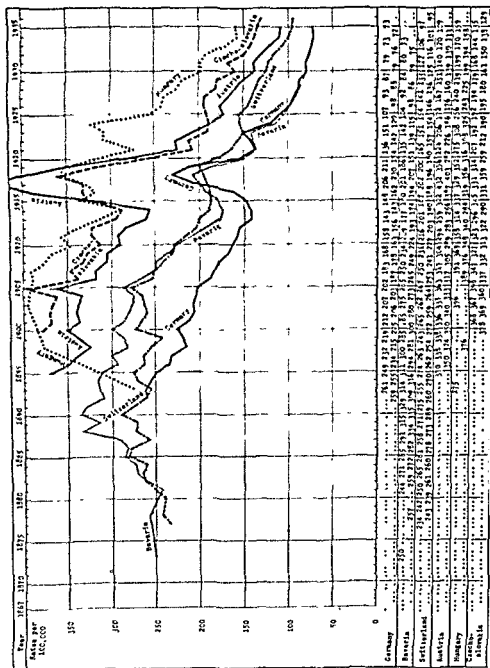


Fig. 3.



influenza pandemic in 1918, but in these instances the levels attained were quickly left behind and were mere accidental interruptions in the more natural long term trends of the disease under ordinary conditions.) More recent instances of places where the epidemic of tuberculosis continues to rise include notably the Philippines and Puerto Rico, where apparently the crest has not even been reached (see Figs. 2, 3, 4, 5 and 6).

EVOLUTION OF TUBERCULOSIS MORTALITY  
IN CERTAIN EUROPEAN COUNTRIES  
AS RECORDED IN GERMANY, BAVARIA, SWITZERLAND, AUSTRIA, HUNGARY AND CZECHOSLOVAKIA



From Epidemiological Reports, Health Section, League of Nations.  
Charted by G. J. Drolet, New York Tuberculosis and Health Association.

Besides examples which may be cited of a tuberculosis epidemic for countries as a whole, there are available records showing the spread within a single one from the population centers to more distant and rural sections. The most striking probably is that reported in Scandinavia, especially in Norway, between 1881 and 1911 (see Fig. 7). In just thirty years a high death rate first prevailing in the more populated southern communities spread gradually to the northern sec-

**EVOLUTION OF TUBERCULOSIS MORTALITY  
IN CERTAIN COUNTRIES  
AS RECORDED IN THE UNITED STATES, AUSTRALIA, NEW ZEALAND, JAPAN, URUGUAY, PUERTO RICO AND THE PHILIPPINES**

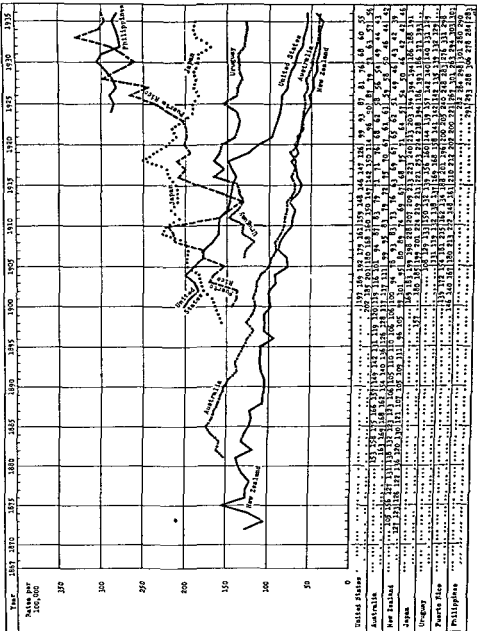


Fig. 5.

From Reports, U S Census Bureau, League of Nations and health authorities,  
Puerto Rico and the Philippines

Charted by G. J. Drolet, New York Tuberculosis and Health Association.

tions. Similarly, in Sweden, as is so well brought out by Neander (see Fig. 8), between 1801 and 1916 the tuberculosis wave, first striking Stockholm and other southern centers of population, has gradually spread to Norbotten where lately the death rate of almost one hundred years ago is now prevailing.

Evidences of the decline of the tuberculosis mortality wave are common, of course, in practically all civilized countries, or at least those where urbanization and industrialization have been highly developed for some time. Since 1900 alone in the United States, for instance, the tuberculosis death rate has fallen from 202 to 43 in 1942, or by 79 per cent (see Table I for the United States, and Fig. 9 for England and Wales since 1851).

Instances of recurrence in communities or in certain groups are as real, but records more difficult to get at. Historical records would indicate that in Egypt tuberculosis was fairly common in some of its populous centers. Then, with the disappearance of its important and older cities, agricultural life became again the pursuit of a greater proportion and tuberculosis probably less prevalent, but nowadays when the Fellaheen or rural worker goes back to towns he is extremely susceptible to acute or general types of the disease and suffers high mortality rates. Woods-Hutchinson, a few years ago, mentioned instances in the United States of New England stock which having gone as pioneers to the open West upon its return to the East, especially in educational centers, provided victims

#### NORWAY — TUBERCULOSIS DEATH RATE\* SINCE 1867

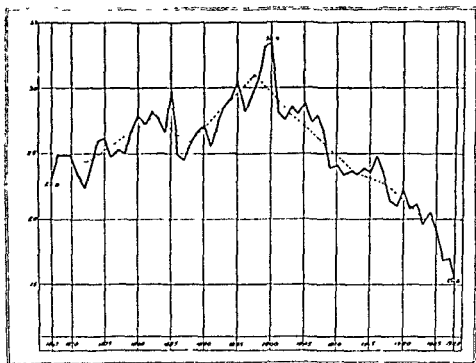


Fig. 6

\*Per 10,000 inhabitants, for all forms of tuberculosis. From Heitmann, Features of Tuberculosis Campaign, Norway, Bull. Internat'l Union Against Tuberculosis, January, 1931, p. 24.

## TUBERCULOSIS MORTALITY, NORWAY

1881-1885, 1896-1900 AND 1911-1915

THIRTY-YEAR PROGRESS OF EPIDEMIC FROM SOUTH TO NORTH\*

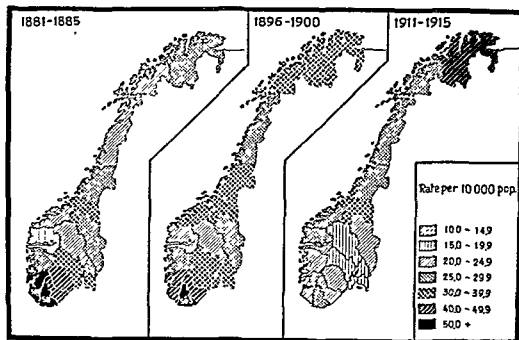


Fig 7.

\*Tuberculosis in Denmark, Norway and Sweden, by Ostenfeld, Heitmann and Neander, Health Organization, League of Nations, p. 78, 1931.

that ran a hasty type of consumption little expected ordinarily in these Anglo-Saxon individuals. In New York City, in the 1860's, tuberculosis death rates were uncommonly high among older age groups of the population. On the other hand, mid-way between that date and the present time, tuberculosis was raging especially among the comparatively young for a while, but during the past few years it is again rather among older men in New York City that tuberculosis death rates above the average are found.

The widespread dissemination of tuberculosis is common knowledge, but the toll of lives taken is not always realized. In the United States alone, since 1900, a comparatively short span of life after all, almost five million have succumbed prematurely to the tubercle bacillus. In twenty countries for which the writer has available the vital statistics records during the forty-year period 1881-1921, it was medically certified that altogether 18,420,450 persons died from pulmonary tuberculosis.

Even with the present and comparatively low rates of tuberculosis mortality prevailing these days, the writer estimates that in the entire world tuberculosis still causes more than two million deaths in a single year.

**Importance.**—The previous remarks indicate that the relative importance of tuberculosis varies with the times, places and, as is well known, among certain groups also. At the present time, in the United States, tuberculosis ranks in the

## TUBERCULOSIS MORTALITY IN SWEDEN\*

A CENTURY'S RECORD OF THE PROGRESS OF THE EPIDEMIC WAVE FROM THE MORE POPULATED CENTERS TO THE RURAL NORTH

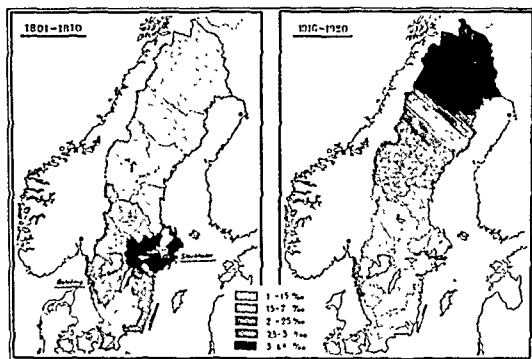


Fig. 8

\*Neander, G. (*Acta tuberculosa Scandinavica*, 1928)

seventh place among leading causes of death and was responsible in 1940 for 60,428 deaths of a grand total of 1,417,269 deaths from all causes; 4 per cent of the total (see Table II). Only a generation ago, in 1910, tuberculosis headed the mortality lists, being charged with 86,309 deaths in the Registration Area in a total of 805,412 deaths from all causes, or 11 per cent of the total.

While at the present time in the United States tuberculosis is responsible, on an average, for one death in twenty-five from all causes of mortality, this proportion is not uniform throughout life. Among children under five years of age, it is only 1 per cent. This ratio, however, rises very quickly and differently in the two sexes; among boys 5 to 15 years of age, tuberculosis causes 4 per cent of all the deaths; but, among girls 10 to 15, it is responsible for two and one-half times as great a proportion, namely, 10 per cent. Among adult men, it causes 16 per cent of all the deaths between the ages of 20 and 30; this decreases slightly between the ages of 30 and 40 and is responsible for only 6 per cent of the deaths in the group 50 to 60 years of age; thereafter, the proportion falls rapidly being under 3 per cent after age 60. The drop among the latter does not imply, however, a lower tuberculosis death rate at that period of life for, as a matter of fact, a peak in the tuberculosis death rate is reached at a comparatively late age among men, but the proportion to all deaths is lowered by the many other causes then prevailing (see Table III). In the female sex, the ratio of deaths from tuber-

# TUBERCULOSIS DEATH RATE\* ENGLAND AND WALES SINCE 1851

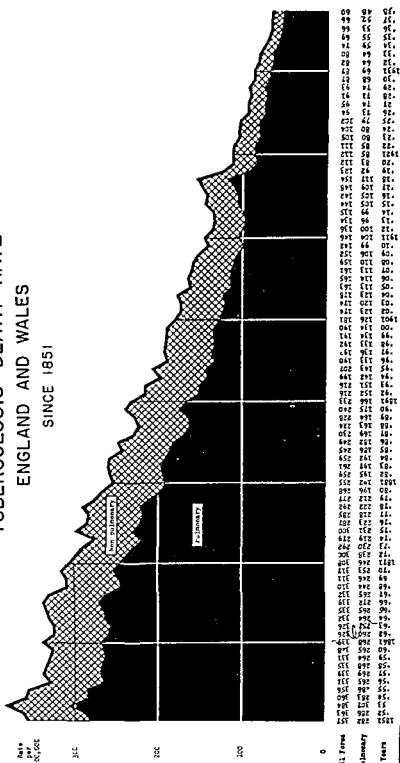


Fig. 9.

\*Mortality from all forms of tuberculosis per 100 000 population standardized for similarity of age and sex composition. From reports of the Registrar-General.

TABLE I  
TUBERCULOSIS MORTALITY IN THE UNITED STATES SINCE 1900\*

Year	Deaths, All Forms		Rate per 100,000		
	Registration Area	Entire U. S.†	Pulmonary	Other Forms	All Forms
1900	62,096	153,781	182	20	202
1901	61,767	153,162	176	21	197
1902	59,083	146,826	161	21	185
1903	61,640	153,059	167	22	189
1904	66,921	166,029	178	23	201
1905	65,478	161,701	168	24	192
1906	75,648	154,507	157	23	180
1907	76,759	156,545	156	23	179
1908	78,409	149,643	146	22	168
1909	81,835	146,013	139	22	161
1910	86,309	147,627	140	20	160
1911	91,205	148,955	138	21	159
1912	90,360	142,646	130	20	150
1913	93,421	142,838	128	20	148
1914	96,903	143,953	128	19	147
1915	98,194	145,010	128	18	146
1916	101,396	143,076	124	18	142
1917	110,285	150,191	129	18	147
1918	122,249	155,381	133	17	150
1919	106,985	132,304	111	15	126
1920	99,916	121,459	101	13	114
1921	88,135	107,126	86	13	99
1922	90,452	105,478	84	12	96
1923	90,732	103,730	81	12	93
1924	89,724	101,882	78	12	90
1925	89,268	99,934	76	11	87
1926	91,568	101,383	76	11	87
1927	87,567	95,739	71	10	81
1928	90,659	94,691	70	9	79
1929	88,352	92,360	68	8	76
1930	84,741	88,010	63	8	71
1931	81,395	84,521	61	7	68
1932	75,509	78,484	56	7	63
1933	74,842	74,842	54	6	60
1934	71,609	71,609	51	6	57
1935	70,080	70,080	50	5	55
1936	71,527	71,527	51	5	56
1937	69,324	69,324	49	5	54
1938	63,735	63,735	45	4	49
1939	61,606	61,606	43	4	47
1940	60,428	60,428	42	4	46
1941	59,251	59,251	41	3	44
1942	57,690	57,690	40	3	43

\* From Mortality Statistics, U. S. Bureau of the Census, and, Whitney, J. S., Facts and Figures about Tuberculosis.

† Figured by applying death rate in Registration Area to population of entire Continental United States.

Note: In 1900, the Registration Area covered only 40.5% of the population numbering in the entire United States 76,129,408; in 1910, 58.3% of 92,267,080, in 1920, 82.3% of 106,543,031; in 1930, 96.2% of 121,091,000; beginning 1933, entire Continental United States, population, 1940, 131,970,224.

culosis to all other causes is highest among young women 20 to 30 years of age, this disease being then responsible in the United States for 26 per cent of all the deaths at that period of life.

**Morbidity.**—The actual morbidity or number of living cases of tuberculosis, a disease which, with its several forms, may, as in many other infections, present

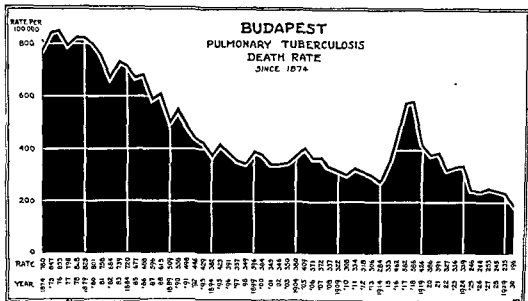


Fig. 10.

Figures by courtesy of Hungarian State Commission for Prevention of Tuberculosis.

**TABLE II**  
**LEADING CAUSES OF DEATH IN THE UNITED STATES, YEAR 1940**

Rank	Cause of Death	Number of Deaths	Death Rate per 100,000*
1	Heart diseases	385,191	292
2	Cancer, all forms	158,335	120
3	Cerebral hemorrhage, diseases of the arteries	145,504	110
4	Nephritis, all forms	107,351	81
5	Accidents, homicide	105,093	80
6	Pneumonias	72,368	55
7	Tuberculosis, all forms	67,428	46
8	Debility, premature birth	58,822	45
9	Diabetes	35,015	27
	Other causes	289,162	219
	All causes	1,417,269	1074

\* Population, Continental United States, 131 970,224 Based on reports, United States Bureau of the Census

every type of case from the mildest to the severest, cannot be accurately stated or else would demand the use of many classifications; but the required registration in most of the States furnishes a fair basis of the probable number of frank, clinical cases, or of those with more or less obvious symptoms. For the year 1942, various State Departments of Health reported, according to Dempsey of the National Tuberculosis Association, that in 48 states of the Union and the District of Columbia a total of 108,555 new cases of tuberculosis were registered. In England and Wales, according to the Ministry of Health, 54,929 new cases of tuberculosis were "notified" during the year 1940. These figures of new cases only do not include known living cases registered in prior years. According to practical experience in communities surveyed by the Committee on Administrative



TABLE III  
PROPORTION OF DEATHS FROM TUBERCULOSIS TO THOSE FROM ALL CAUSES, BY SEX AND AGE  
*United States, Year 1930*

Age	Male			Female			Both Sexes		
	Deaths		Per Cent Tbc	Deaths		Per Cent Tbc	Deaths		Per Cent Tbc
	All Causes	Tuber- culosis		All Causes	Tuber- culosis		All Causes	Tuber- culosis	
All ages	791,003	35,795	5%	626,266	24,633	4%	1,417,269	60,428	4%
0-5	77,039	800	1%	58,623	743	1%	135,662	1,543	1%
5-9	6,638	247	4%	4,932	222	5%	11,570	469	4%
10-14	6,758	300	4%	4,925	475	10%	11,683	775	7%
15-19	11,735	1,215	10%	9,333	2,169	23%	21,168	3,375	16%
20-29	32,172	5,231	16%	26,354	6,764	26%	58,526	11,995	20%
30-39	41,975	6,233	15%	34,274	4,990	15%	76,249	11,223	15%
40-49	73,491	7,487	10%	51,794	3,173	6%	125,285	10,660	9%
50-59	123,153	7,111	6%	78,140	2,356	3%	201,293	9,467	5%
60-69	160,732	4,612	3%	115,192	1,974	2%	275,924	6,616	2%
70-79	161,491	2,080	1%	138,049	1,355	1%	299,540	3,435	1%
80+	94,758	406	0.4%	103,909	395	0.4%	198,667	801	0.4%

Note. Total includes 1,702 deaths of age unknown of which 69 were due to tuberculosis. Based on reports U. S. Bureau of the Census.

Practice of the American Public Health Association, there are, on an average, two new cases reported during a given year for each death, and a total of five cases of clinical tuberculosis on a given day in a community to each one death occurring during the year. In the entire United States, with more than 57,000 tuberculosis deaths annually, there are still approximately between 285,000 and 300,000 cases of tuberculosis of all types: acute, chronic, with possibly a certain number of quiescent cases able to do some work but yet listed in the registers for observation or supervision since many continue to have a positive sputum.

**Incidence.**—The determination of the present prevalence of tuberculosis, either as a mere infection or as active disease, depends especially upon three types of records: first, those that reveal, primarily through tuberculin testing, the frequency of infection or rather the number already infected; secondly, morbidity records, primarily those available through registration, especially of clinical cases; finally, the more definite mortality records, which, because of a continuing tendency to maintain a constant ratio to living cases, are likewise a parallel index of the existing number of cases. To these might be added necropsy records and, for that matter, the incidence of pulmonary lesions demonstrable through the x-ray, the last is more definite when accompanied by the tuberculin test, especially the Mantoux method.

#### PREVALENCE OF INFECTION.

Records of the incidence of tuberculous infection, as revealed through tuberculin testing, deal primarily with findings during childhood or adolescence since in urbanized communities ultimately most of the adults are found to be infected, though this condition is not as universal as it was once deemed. Certainly in the United States, where far-reaching campaigns for the control of tuberculosis both bovine and human have been pushed actively, a fairly large proportion

**TREND OF MORTALITY FROM TUBERCULOSIS  
(ALL FORMS)  
IN CERTAIN LARGE CITIES**

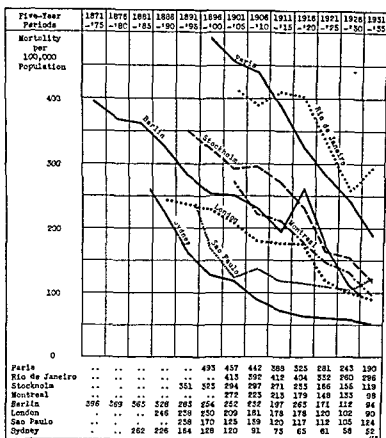


Fig 11

(From Monthly Epidemiological Report, Health Section, League of Nations)

of young adults are now being found, on entrance to colleges and universities, to be still uninfected. Likewise, in rural sections or where some people still live a more primitive life, especially in Africa, a goodly proportion of adults may be found to be free from any infection upon first coming into contact with life in towns, or industrial and mining places.

The fact, however, that certain groups present similarities in the proportion reacting to tuberculin and, therefore, revealing infection is not necessarily a complete measure of tuberculosis among them. As Miller and Rappaport<sup>3</sup> have remarkably well put it lately there are in individuals and in certain groups or communities levels or degrees of tuberculization that have far-reaching influences modifying the eventual course of the infection or progress of manifest disease. These reveal themselves under appearances which at times one may term as immunity and on other occasions as susceptibility. Their acquirement and status are not only governed by the circumstances in the individual's life but are interrelated with the entire history of the stock from which he springs.

The extent of tuberculous infection, it is well known, is affected by a number of factors among which is, first of all, that of age; secondly, urbanization, eco-

nostic conditions and contact with open cases. Sex, race—under similar conditions—and season do not modify significantly the incidence of infection.

**Among Infants.**—There are relatively few representative records of the frequency of tuberculous infection among infants in large centers of population, especially that have been obtained through the Mantoux or intradermal tuberculin test rather than the less accurate, former von Pirquet; still, enough are at hand to visualize the probable limits of infection.

In San Francisco, Dickey and Seitz<sup>4</sup> reporting from their findings in the Children's Clinic at Stanford for the years 1925-28, state that, among 179 children "one year of age," 5.6 per cent reacted positively. Asserson,<sup>5</sup> in New York City, during the period 1920-26 studied hospital, clinic and baby health station records and reported that in 4003 infants under two years of age, which included a number of cases of clinical tuberculosis at the Nursery and Child's Hospital and in the Babies' Hospital and Clinic, 11.4 per cent reacted. Taking, however, clinic cases alone, 840 of them under two years of age, she found that only 4.5 per cent reacted to intracutaneous tests, furthermore, 816 well babies seen at different baby health stations revealed only 1.3 per cent reactors. More recently, in New York City also, the writer, thanks to the courtesy of Doctors C. H. Smith, H. W. Dargeon and L. C. Schroeder, had access to their records in the children's wards at Bellevue, St. Luke's, and the Nursery and Child's Hospital for the years 1930 to 1932. Among 1789 infants tested during the first year of their life, only 4.3 per cent reacted (Several years ago Fishberg, in New York City, found a higher proportion reacting.) Also, in clinics generally limited to the examination of members of families from tuberculosis cases, and therefore the majority of them contacts, a greater proportion, though still lower than might be expected, were found already infected.

It is obvious, however, that concurrently with the active and widespread anti-tuberculosis campaigns in America both by official health authorities and under private auspices that, even in densely populated centers like New York City, only a comparatively small proportion of infants in the general population are now infected. With only 4 per cent of infants reacting among those tested on general hospital services, and probably a still smaller proportion among those at home, there is an indication of the far-reaching control of tuberculosis at that most susceptible age which has been attained here.

**Pre-School Age.**—Among children of pre-school age, two to six years old, the proportion found infected in New York City ranges between 10 and 16 per cent, at least in the general hospital group studied by the writer. A few years ago Smith<sup>6</sup> found it to be between 16 and 19 per cent. In San Francisco, Dickey and Seitz<sup>4</sup> report for the same age group between 14 and 20 per cent reactors; in London, Dow and Lloyd,<sup>7</sup> approximately 25 per cent; and Hart,<sup>8</sup> in the age group three to six in the same city, between 11 and 18 per cent.

**School Children.**—Among school children, at least those between the ages of 5 and 15, a number of surveys in large cities are available which indicate the present frequency of tuberculous infection. Somewhat higher proportions than elsewhere were reported for Philadelphia by Hetherington, McPhedran, Landis and Opie,<sup>9</sup> than have been found in London by Dow and

TABLE IV  
PERCENTAGE OF CHILDREN UNDER FIFTEEN REACTING TO INTRACUTANEOUS TUBERCULIN TESTS  
FROM SURVEYS IN SEVEN GREAT CITIES

Place.	New York City 1930-1932	Chicago, Illinois 1930-1931	Phila- delphia 1926	Detroit, Michigan 1929	Minne- apolis 1926	San Fran- cisco 1925-1928	London, England 1930-1931
Date ..							
Children	8,045	1,000	2,678	2,467	2,045	3,500	1,003
Authors	(10)	(Webb)	(9)	(Johnston)	(11)	(4)	(7)
Age:							
0-1 yr.	4.4	3.5		1.7			
1-2 yrs.	8.2	7.9		7.5		5.6	0
2-3 yrs	10.6	5.8		4.0		13.6	12.9
3-4 yrs	12.8	9.0	40.0	7.0		16.9	30.8
4-5 yrs	16.0	8.8	42.1	14.3		19.8	24.6
5-6 yrs	14.5	13.0	37.7	13.3		20.6	24.4
6-7 yrs.	14.1	10.0	43.1	12.6	20.8	16.5	44.3
7-8 yrs	17.3	10.7	47.7	16.0	27.4	16.1	40.6
8-9 yrs	23.1	14.4	62.2	17.0	38.9	26.4	42.0
9-10 yrs	23.7	23.6	63.5	18.1	41.1	27.7	46.2
10-11 yrs	30.4	23.6	70.9	22.4	50.6	26.2	47.3
11-12 yrs.	31.1	22.6	73.1	15.3	50.0	38.0	54.4
12-13 yrs.	29.2	16.1	77.6	16.7	59.7	39.1	66.7
13-14 yrs.	44.1	21.1	77.9	28.3	58.4	42.2	55.0
14-15 yrs	42.1	30.5	79.9	16.7	69.5	46.6	82.2
0-5 yrs	9.2	7.6	41.7*	6.9		15.1†	23.0‡
5-10 yrs.	18.1	14.0	54.2	15.5	34.9†	20.9	39.0
10-15 yrs	31.4	22.3	76.6	19.2	56.8	36.9	58.3
0-15 cru §	13.6	14.5	68.5*	14.1	47.3†	23.5‡	43.1‡
0-15 adj §	19.2	14.4	61.0*	13.6	46.8†	24.6‡	40.8‡

\* Beginning with those 3 years old only † From 6 years on. ‡ From one year on.

§ Crude percentage for the entire group in each city, where obviously different proportions of children of various ages were tested. Adjusted, by applying the specific ratios of each age group to a common, comparable child-population, namely, that of the children in the standard million of England and Wales for 1901; under five, 114,212, five to ten, 107,209, ten to fifteen, 102,735. Thus in New York City, the percentage found reacting would indicate 62,176 infected in the total under fifteen of 324,206 children in the standard million—or 19.2 per cent positive. In Philadelphia, 155,478 infected among 254,730 aged three to fifteen—61.0 per cent. Similarly, for Minneapolis figures of only the children aged six to fifteen in the standard million, as in the group tested, were utilized; for San Francisco and London, the fraction under one year was excluded.

Lloyd,<sup>7</sup> or Hart,<sup>8</sup> and by the writer,<sup>10</sup> in New York City. For the first place, the age group five to ten was said to furnish 54 per cent reactors, those 10 to 15, 77 per cent; in London, in the first instance, 39 per cent reactors in the age group five to ten and 58 per cent among those 10 to 15; in the second instance, Hart's series, in a group of children six to ten inclusive, 32 per cent was the average. In New York City, the writer's survey for 1930-32 disclosed 19 per cent reacting in the age group five to ten and only 29 per cent for the combined group 10 to 15 though here, it should be added, there was a concentration of children around 11 and 12. An equally low proportion of reactors has been noted elsewhere, for instance, by Dickey and Seitz<sup>4</sup> in San Francisco where the children five to ten showed 21 per cent infected and those 10 to 15, 37 per cent only. Smith,<sup>6</sup> for the period 1921-28 in the Bellevue Hospital series, found, for children of school age, from 26 to 43 per cent of reactors as they grew older. In Minneapolis, Harrington and Myers<sup>11</sup> found among children five to ten years of age

35 per cent reacting and among those 10 to 15, 57 per cent. Whitney and McCaffrey,<sup>12</sup> reporting on non-contact children tested with purified protein derivative in the 1934-36 investigation of the National Tuberculosis Association extending over 30 States and the District of Columbia, found 19 per cent reactors among children five to ten years of age and 31 per cent among those 10 to 15— with much higher proportions among a similar group of contacts.

The frequency of infection among school children in other communities, especially of smaller size than the great metropolitan centers, should, at least in the United States, probably be less than those mentioned just now. It is probable that here the rapid decline of tuberculosis mortality and the steady increase in the segregation of advanced cases in hospitals or sanatoria are radically altering the picture as far as general infection is concerned during childhood and adolescence.

**Among High School and University Students.**—It has generally been held that by the time adolescence is reached the greater proportion at that age are already infected with tuberculosis, but while this might be so in great centers of population it is not necessarily the case in smaller communities or in colleges and universities in the United States that draw from all parts of the country including rural sections. In Philadelphia, at the University of Pennsylvania, Hetherington, McPhedran, Landis and Opie<sup>13</sup> found among high school students that in a group between 16 and 17 years of age 79 per cent reacted to the intracutaneous test; among the college students, between the ages of 19 and 20, 82 per cent; and among medical students, probably more exposed to infection than others, of those 24 years of age, 95 per cent were already infected. But at Yale, New Haven, Soper and Wilson<sup>14</sup> found much less tuberculous infection. In the entering class of 1931, among 838 undergraduates averaging in age 19 years, 46 per cent were still negative; in the graduate schools, with average age slightly over 24 years, the percentage positive was only 68, though among the medical students it was 77 per cent.

Variations to be found as to infection among high school students are illustrated, for instance, at Rochester, Minnesota, where Hewitt and Cutts,<sup>15</sup> in the entire student body of 1565, found only 11.5 per cent reactors. In Minnesota, also, in the high schools of Morrison County, Leggett<sup>16</sup> tested 376 students ranging in age between 12 and 20 and found only 15 per cent of reactors. On the other hand, in a community with a fairly high tuberculosis death rate, Honolulu, Hawaii, Doolittle<sup>17</sup> found in the junior high school students, averaging in age between 14 and 15, 75 per cent already infected, but it should be remembered that the greater proportion of the students there included a large number of children of Oriental extraction. In Michigan, at the Central State Teachers' College at Stevens Point, Dearholt<sup>18</sup> reports, among 395 students Mantoux

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*Note:* In the New York City series quoted, while the hospital children, ten to fifteen years of age, that were observed showed only 29 per cent reacting, in another series of children of the same age attending tuberculosis clinics and among whom there was said to have been no history of contact, the reactors averaged 44 per cent. It is probable that the last figure is more representative of infection among school children in this upper age group; but it would still indicate, that lately a substantial proportion are not as yet infected till adolescence or adult life even in a congested center like New York.

tested, only 39 per cent reacting, the proportion being even lower among young women (32 per cent) but higher among young men (52 per cent).

The most significant data with regard to the prevalence of tuberculous infection in students in American colleges following a test with standardized tuberculin are those reported by Long and Seibert<sup>19</sup> in the cooperative study by the Henry Phipps Institute, the College Hygiene Association and the American Student Health Association (see Table V).

**Among Adults.**—With regard to the prevalence of infection in adult life, at least in a congested urban community, Kereszturi *et al.*<sup>20</sup> report finding among older men, residents of the New York City Farm Colony, between the ages of 40 and 92, 100 per cent positive reactors in the group 40 to 50; 95 per cent on a single test with 0.1 mg. of O.T., among those 50 to 80 years of age; and, in those 80 and over, 100 per cent reactors.

**Sex.**—Generally no significant differences between the two sexes as to the frequency of tuberculous infection are revealed in the various surveys where data have been made available separately for each; most surveys would indicate that both sexes are usually fairly equally infected. In Philadelphia, Hetherington, McPhedran, Landis and Opie,<sup>9</sup> reported, among school children, 75 per cent reactors among those of the female sex and 72 per cent of the male sex. Dickey and Seitz,<sup>4</sup> in San Francisco, found among comparatively young children, that those of the male sex showed 23 per cent reacting and, of the female, 24 per cent. In New York City, the writer found, from the hospital records made available by the courtesy of Doctors Smith, Schroeder and Dargeon,<sup>10</sup> 13 per cent reactors among the male children and 15 per cent among the female. Barnard, Amberson and Loew,<sup>21</sup> testing adolescents in Bellevue-York-

TABLE V

A.—INCIDENCE OF POSITIVE TUBERCULIN REACTIONS (PURIFIED PROTEIN DERIVATIVE) IN WHITE AMERICAN COLLEGE STUDENTS (CHIEFLY NEW ENTRANTS) IN 1935-1936, MALE

College	Physician	Number Tested	Average Age	Per Cent Pos.
Yale University	Soper	1,311	20.06	46.4
Rutgers University	Kler	397	17.93	48.9
University of Pennsylvania	Lees	1,045	18.93	48.8
Haverford College	Taylor	181	17.46	65.7
Emory University	Blackford	120*	22.54	48.3
Pennsylvania State College	Ritenour	857	18.97	40.7
Ohio Wesleyan University	Blydenburgh	271	19.68	28.0
University of Wisconsin	Stiehm	2,123	18.97	30.8
Iowa State College	Edwards	1,120	17.72†	21.4
University of Kansas	Canuteson	912	19.34	35.1
University of New Mexico	Werner	185	22.02	72.7
N. Mex. State Teachers College	Werner	69	24.95	81.1
Six Idaho colleges	Several	341	.....	22.5
University of Oregon	Hayes	579	19.55	49.9
Stanford University	Shepard	708	19.84	45.0
San Jose State College (Calif.)	Mason	84	19.44	67.8
Compton Junior College (Calif.)	Smart	365	18.30	44.6
University of Calif. (Berkeley)	Legge	1,259	17.36	33.6
University of Calif. (Los Angeles)	MacKinnon	213	20.25	57.7
		12,140		

\* Medical students only. † Positive reactors only.

B.—INCIDENCE OF POSITIVE TUBERCULIN REACTIONS (PURIFIED PROTEIN DERIVATIVE)  
IN WHITE AMERICAN COLLEGE STUDENTS (CHIEFLY NEW ENTRANTS)  
IN 1935-1936, FEMALE

College	Physician	Number Tested	Average Age	Per Cent Pos.
Yale University	Soper	190	23.99	57.9
University of Pennsylvania	Lees	184	18.51	42.9
Bryn Mawr College	Leary	416*	19.5	46.5
Pennsylvania State College	Ritenour	302	20.47	42.7
Ohio Wesleyan University	Blydenburgh	460	18.73	23.8
University of Wisconsin	Stiehm	1,128	19.41	24.6
Iowa State College	Edwards	330	21.40†	19.1
University of Kansas	Canuteson	396	19.05	25.3
University of New Mexico	Werner	144	25.11	68.7
N. Mex. State Teachers College	Werner	86	22.55	79.0
Six Idaho colleges	Severall	527		15.3
University of Oregon	Hayes	476	19.33	46.8
Stanford University	Shepard	325	19.55	30.7
San Jose State College (Calif.)	Mason	202	20.94	44.5
Compton Junior College (Calif.)	Smart	397	18.08	35.7
University of Calif. (Berkeley)	Legge	1,041	17.42	29.0
		6,604		

\* All college classes. † Positive reactors only.

ville, New York City, reported 69 per cent reacting boys and 66 per cent reacting girls; in London, Dow and Lloyd,<sup>7</sup> 41 per cent male and 46 per cent females; in Honolulu, Doolittle,<sup>17</sup> among junior high school students, 78 per cent among the males and 71 per cent among the females; in Minneapolis, Harrington and Myers,<sup>11</sup> among school children, 49 per cent males, and 46 per cent females. Whitney and McCaffrey,<sup>12</sup> in their group, largely school children, found practically the same proportion of reactors in the two sexes, 48.3 among males and 45.9 among females. The same authors<sup>22</sup> report from tuberculin testing with MA-100 among native-born persons, mostly under 20 years of age, 25 per cent positive in the male sex and 23 in the female. The Tuberculosis Committee of the American Student Health Association<sup>23</sup> found a fairly close approximation in the proportion of the two sexes reacting to tuberculin testing in the school year 1936-1937, 29 per cent of the men being positive and 25 per cent of the women. Long and Seibert<sup>10</sup> likewise report a nearly similar proportion of reactions among male and female students tested in 1935-1936 with purified protein derivative. They noted, however, a slightly higher percentage of reactors among female students: 58 per cent at Yale University among the women against 48 per cent in the men; the former, however, averaged 24 years of age as against 20½ in the latter. Although the fact remains that the mortality rates in the two sexes at various periods of life are markedly unequal, there is no general evidence, at least during the earlier part of life, that one is significantly infected more frequently than the other.

**Urbanization.**—Opportunities for infection are, of course, far more numerous in cities than in rural communities. A number of investigations during the past decade are available as to the extent of tuberculous infection prevalent in certain large centers of population. These surveys certainly do not all show necessarily that a high proportion are infected early in life as was first thought

from earlier European records. Dealing with investigations, fairly recent, one finds, while the percentage of infection rises with age and opportunities for exposure, that the record in certain representative places is somewhat as follows: In Philadelphia, Hetherington, McPhedran, Landis and Opie,<sup>9</sup> in 1926, among school children, noted that by the age of 15 evidence of infection was found in 80 per cent; in New York City, Barnard, Amberson and Loew,<sup>21</sup> among adolescents, 13 to 14 years of age, on the East Side, found 67 per cent reacting; the writer,<sup>10</sup> from hospital records in the children's wards in three important general institutions in New York City for the period 1930-32, which covered 6082 children, found that of children under five years of age 9 per cent reacted, and, among those 14 to 15, 67 per cent. In London, Dow and Lloyd,<sup>7</sup> in 1930 in the hospital series previously mentioned, reported 23 per cent reacting under five years of age, and 82 per cent among those 14 to 15 years of age. Hart,<sup>8</sup> in the same city, in 1929, in a group of some 751 clinically non-tuberculous children, reports 7 to 18 per cent among those under five years of age, and 41 to 70 per cent in the group 10 to 15. In Honolulu, Doolittle,<sup>17</sup> in 1930, among junior high school students, a group 10 to 15 years of age, found 75 per cent reacting. As already stated much lower percentages of infection were reported in San Francisco by Dickey and Seitz,<sup>4</sup> among children in a hospital clinic; the group 14 to 15 years of age showing only 47 per cent reacting. In Minneapolis, Harrington and Myers,<sup>11</sup> a few years ago, reported 51 per cent in those aged 14 to 15 years. All of the surveys just noted were made with intracutaneous injections of tuberculin.

The influence of urbanization may also be discerned in the higher percentage of college students found reacting in institutions located in the more congested, populous eastern seaboard of the United States. Thus, the report of the Tuberculosis Committee of the American Student Health Association<sup>23</sup> shows an average of 52 per cent positive among students in the New England States as against, for instance, 27 per cent in those in the States of the Mississippi Basin. Higher rates in the Mountain States must, of course, be due to the fact that these sections have always attracted health seekers, especially tuberculosis cases.

**Rural Conditions.**—Several surveys within the past few years have been reported for rural sections of Canada or the United States. In Ontario, the Canadian Tuberculosis Association,<sup>24</sup> from a survey in 1923 among school children, reported in the group 10 to 15 years of age 41 per cent reacting; Korns,<sup>25</sup> in Cattaraugus County, New York, only 11 per cent for those of the same age group; Slater,<sup>26</sup> in Minnesota, with the von Pirquet test, reported a percentage of reactors not reaching more than 12 per cent among school children.

It should be noted in some of these rural communities with a comparatively small percentage of reactors, even among adolescents, that on the other hand the proportion infected is fairly constant even among the younger children. It would seem to suggest that in these places the main source of infection is bovine rather than human. In Minnesota, again, Leggett and Myers,<sup>16</sup> in 1930, reporting on high school children in rural sections, found only 19 per cent reacting. In North Carolina, in 1927, McCain,<sup>27</sup> among some 25,000 school children, found that the average proportion of reactors was 23 per cent. Further south, Aronson.<sup>28</sup>



following the careful methods of the Phipps Institute, would seem to have found in rural communities of Tennessee and Mississippi a higher percentage of reactors—these sections have, however, an unusually high proportion of Negroes. In Gibson and Lake counties of Tennessee, among the whites, 10 to 15 years of age, 60 per cent reacted and among the colored, 65 per cent.

**Contact.**—Opportunities for contact, especially with open cases of tuberculosis, are the most prolific source of infection. Data of recent surveys are available in a number of instances; all indicate, depending probably upon the intimacy of the contact and perhaps the general prevalence of tuberculosis in the community, that a very great excess of children or persons are found infected among those exposed compared with those not so endangered. In general, however, this difference of infection between contacts and non-contacts is much greater in early childhood than later in life. In Philadelphia, Opie and McPhedran,<sup>29</sup> reporting on a group tested in 1926, found among children under five years of age 80 per cent of the contacts already infected as against 23 per cent for those with no known history of contact; among those 10 to 15, however, instead of a four to one ratio it was two to one, namely, 91 per cent reacting among contacts and 46 per cent among non-contacts. In New York City, Barnard, Amberson and Loew,<sup>21</sup> among adolescents found 86 per cent reacting among contacts and 67 per cent among non-contacts. The writer,<sup>10</sup> studying some 6646 records in the children's sections of tuberculosis clinics where, however, a number are brought for examination who occasionally come from non-tuberculous families, found among those under five years of age 41 per cent reacting among contacts and 28 per cent among non-contacts; in the age group 15 to 20, however, the proportion was almost equal in each group, 70 and 69, respectively. In New York, again, the records of Dr. Dargeon, of St. Luke's Hospital, for 1631 children in the general wards of that institution showed in the age group five to ten, 27 per cent reacting among contacts and 13 per cent among non-contacts; among those under five, however, 48 per cent to 6 per cent. In London, Dow and Lloyd<sup>7</sup> report similar findings, 40 per cent reacting in the contact group to 20 per cent in the non-contact. In Minnesota, Slater,<sup>26</sup> among school children, reports 86 per cent of the contacts reacting to 13 per cent of the non-contacts. Hart and Schlesinger,<sup>8</sup> London, in a group zero to 15 years of age report 62 per cent among contacts to 24 per cent among non-contacts. Among contacts tested with purified protein derivative, Whitney and McCaffrey<sup>12</sup> reported 54.2 per cent positive as against 33.3 among the non-contacts of all ages tested. In children under five, the reactors among the contacts were 40.3 per cent and among non-contacts 13.2 per cent. Obviously, the opportunity for home contact determines largely the percentage of those infected earlier in childhood.

**Color and Race.**—These have not been found to be a significant source of difference in infection, even though evidence is available in a number of places as to the varying mortality rates of certain racial groups. In New York City, Asserson,<sup>5</sup> reporting on some 4000 infants under two years of age tested in hospitals and clinics, found 11.3 per cent reacting among the white babies and 11.5 per cent among the colored. The writer,<sup>10</sup> utilizing the hospital records

made available by Doctors Smith, Dargeon and Schroeder for some 6000 children, found little difference according to color, though in general the tendency was for slightly higher proportions of infection among the colored than among the white. Whitney and McCaffrey<sup>12</sup> in the final report of the National Tuberculosis Association on testing with purified protein derivative state that the percentage of positive reactors among white persons, "adjusted to the population of the United States in 1930," was 46.5 per cent. The Negroes tested showed only 1 per cent more positive reactors, the infection rate "adjusted for age" being 47.8 per cent. It is, however, an open question as to the significance of these minor differences since Aronson<sup>28</sup> has well pointed out the greater sensitivity of Negroes to tuberculin and it may be that the same dosage in the tests may bring out the presence of an infection more readily among those who are more allergic than among those who are not, though both may be as frequently or commonly infected. In Philadelphia, Hetherington, McPhedran, Landis and Opie,<sup>9</sup> among 4107 school children, found that 74 per cent of the white reacted compared with 73 per cent among the colored. In North Carolina, McCain<sup>27</sup> reported 22 per cent white reacting against 27 per cent colored.

Obviously, the greater mortality rate of colored groups than the white can not be explained on the mere score of infection, or at least no convincing evidence so far has been produced to that effect.

Records of infection on the basis of nationality tend to follow the findings according to color. In New York City, Asserson,<sup>5</sup> among the hospital infants mentioned, reported 12 per cent of the colored reacting, 12 per cent of the Italian babies, 11 per cent of the American, 13 per cent of those of Jewish extraction and 16 per cent of the Irish; no material difference therefore. But in the subsequent follow-up of all these babies that she made, the mortality rates became sharply differentiated along the usual lines. In Philadelphia, Hetherington, McPhedran, Landis and Opie,<sup>9</sup> in the school children reported upon previously, found 75 per cent of the Jewish reacting, 68 per cent of the American-born compared with 73 per cent among the colored. In San Francisco, Dickey<sup>30</sup> testing children of Oriental extraction found 32 per cent positive among the Chinese, 35 per cent among the Japanese compared with a somewhat general average in the child population of the city of 25 per cent. In Honolulu, Doolittle,<sup>17</sup> among the junior high school students, did not find a very great difference in the reactions of those of Chinese, Japanese or Portuguese extraction, though the mortality rates of these groups showed some differences. Likewise, in Massachusetts, Chadwick,<sup>31</sup> with the use of the von Pirquet only, classifying the results by nationality records found variations between 25 and 33 per cent only. In Saskatchewan a few years ago, however, at least among Indian children, a very high proportion was found by Ferguson<sup>32</sup> to react, namely 93 per cent, compared with from 40 per cent to 60 per cent in other Canadian or British-born groups. Whitney and McCaffrey<sup>12</sup> report "of the native-born Americans of native parentage, 27.6 per cent evidenced tuberculous infection whereas 38.4 per cent of the native-born of foreign stock and 61.2 per cent of the foreign-born responded with positive reactions when tested with P.P.D." Among Indians, there were 72.4 per cent positive. Korns,<sup>33</sup> also among Indians

of various ages in Cattaraugus County, found 55.4 per cent\* reacting compared with 34.8 in the white population tested. He remarks: "The Indians develop sensitiveness to tuberculin earlier in life, show a higher degree of sensitiveness and a more definite persistence of this sensitiveness until old age." Long and Hetherington,<sup>34</sup> in a survey in the Papago Indian area of southern Arizona, found among children five to ten years of age 62 per cent already reacting. Among Finns of Marquette County, Michigan, Lojacono<sup>35</sup> reports 29.3 per cent positive as compared with 16.3 among non-Finns in the same area.

In striking contrast to the usual findings of tuberculous infection in most places is the experience of Kahn<sup>36</sup> among Upper Aucaner Bush Negroes in Dutch Guiana, in a jungle practically isolated from all contacts. Testing carefully with purified protein derivative Negroes and Indians there, he found among 765 Bush Negroes, most of them adults, only 18 or 2.3 per cent positive reactors; similar tests among 70 Mukuyana Indians were all negative.

**Economic Conditions.**—Authors in Europe have reported finding differences between poor children compared with those of richer groups by following a division of families as to whether they employed servants or not, or other indices of economic strata. Probably similar differences, early in life, would be found between comparatively poor and rich sections here,<sup>†</sup> since it involves in the one instance life perhaps under crowded conditions and on the other hand in more spacious quarters; but play, school, travel and amusement places quickly equalize opportunities for infection.

**Reduction of Incidence.**—With tuberculosis mortality declining, the number of new cases becoming fewer, there must be a lesser incidence of infection. Records of tuberculin testing, on a truly comparable basis as to technic or as to groups investigated, being of comparatively recent date, are necessarily limited. There are, however, already at hand certain significant figures of the changing conditions as to the prevalence of infection. For instance, the Tuberculosis Committee of the American Student Health Association notes that in the school-year 1932-33 the tests showed 35.0 per cent of the students positive; in 1933-34, 30.3 per cent; in 1934-35, 29.4 per cent; in 1935-36, 30 per cent; and in 1936-37, 27.3 per cent. In the United States, between 1930 and 1935, the tuberculosis death rate fell from 71 per 100,000 to 55. Long<sup>37</sup> notes that in a particular Philadelphia high school the pupils tested in 1928 showed 74 per cent reactors among the boys and 90 per cent among the girls. In the same school in 1937, in the first group 68 per cent reacted and among the girls 62 per cent; these children were living in a congested part of the city. Korns,<sup>38</sup> working in Cattaraugus County, the seat of the first of the New York State health demonstrations stimulated by the Milbank Memorial Fund, remarks that for years "tuberculin testing has been a routine procedure for all clinic children under 16." A total of 2621 clinic children tested during the nine years prior to 1937 showed an incidence of 9.2 per cent positive reactions. During the first three years of this

\*Rate adjusted for a similar age composition as that of white population tested.

†Long<sup>37</sup> reports that in Santa Barbara, California, a school with pupils of a high social and economic level had 24.4 per cent reactors whereas another school with pupils of low social and economic level furnished 33.3 per cent reactors.

time the percentage of reactors was 15.6, while during the last six years it was only 4.8. Beaven<sup>29</sup> reports a striking drop in the percentage of reactors tested in the pediatric department of the University of Rochester School of Medicine. In 1926, the incidence of positive reactions among children to old tuberculin was 22.6 per cent; during the three-year period, 1926-28, it was 14.8 per cent; during a similar period, from 1929 to 1931, it was 9 per cent; and, in the period 1932-1934, it was 5.6 per cent. He notes, however, that the mortality rate among infected children has changed little.

**Clinical Significance of Infection.**—Among adults it is fairly common knowledge that the incidence of clinical tuberculosis and infection do not run parallel courses; most have already been infected, and yet varying low proportions only have active disease or die from tuberculosis.

Among children, the clinical significance of infection is still very debatable and the number with manifest disease undoubtedly varies under certain conditions. However, a certain amount of statistical evidence is available to check upon the incidence of disease. First for infants, under ordinary conditions of life, the former views generally based on European observations, as to the *great seriousness and gravity of infection at that age, have had to be modified*. Certainly not all infants infected die of tuberculosis. In New York City, Asserson,<sup>5</sup> in a five-year follow-up of 405 infected infants, including hospital cases, a number with advanced tuberculosis, found that though 209 died, 196 or 48 per cent survived. At the end of five years, of 112 advanced cases 4 per cent were still alive; of 25 with chronic forms (bone and glandular types), 68 per cent; and of 207 without obvious clinical disease, though they had reacted to tuberculin, 61 per cent survived.

The writer, considering the present incidence of tuberculous infection among children under one year of age, in New York also, which from recent hospital experience he found to average 4.3 per cent, figures therefore that among the 123,000 children born in 1930 there may have been in the entire city approximately 5000 infected by the end of their first year of life. But the total mortality of infants certified as due to tuberculosis in a given year recently has usually been less than 75; granting diagnoses incomplete and the reality ten times as great, the larger figure would still be but a fraction of the total number infected. Obviously at present the great majority of infants infected with tuberculosis here survive.

As children become older many more, of course, are infected, and yet it is common knowledge, for instance, that during the period of schooling—from five to fifteen years of age for the majority—that it is at this time of life that tuberculosis mortality is comparatively the lowest. Opie,<sup>40</sup> writing upon the significance of infection among school children, presented evidence for Philadelphia which would show for the age group five to fourteen that 0.6 per cent only required "treatment for clinically manifest tuberculosis of the lungs" either of the childhood or adult type.

Among adults the incidence of clinical tuberculosis depends upon or is modified at present by certain factors: age, sex, race or inheritance, and, probably

within these more or less natural distinctions, economic or occupational factors; also, perhaps by personal habits or intercurrent infections. The writer, considering the entire community, would estimate that at present the prevalence of tuberculosis averages under half of one per cent. Adult males in New York, and somewhat generally in the United States also, now have their highest death rate around age fifty-five; at that period of life, therefore, there is probably one per cent with clinical disease. All male adults may, on an average, show about 0.75 per cent with disease. Among females, with the highest death rate during the age period twenty to twenty-five, the present mortality would indicate probably 0.5 per cent of that group with disease, and possibly lower proportions for the older ones.

Among the colored, with their death rate high, and living clinical cases therefore less numerous because of a more acute course and hastened mortality, the incidence of the remaining manifest cases probably ranges between one and 1.5 per cent.

The latest mortality data are probably the best basis to estimate the number of clinical cases in a given community, with these qualifications in mind. First, that the most reliable reports show an average of five times as many living cases of tuberculosis on a given date as there are tuberculosis deaths in the community annually; into this group should not be read doubtful or border-line cases, nor those with arrested tuberculosis, but simply those with definite disease, that one would conscientiously consider registering as a case with the health authorities. The ratio of remaining living cases to deaths is undoubtedly lower in groups like the colored or other racial strains where the disease runs a more acute course (in America, those of Indian extraction, Scandinavians, French Canadians, Puerto Ricans, Mexicans), probably, therefore, nearer two or three living cases among Negroes or such types to each death. On the contrary, this ratio is greater where the disease tends to chronicity or to be resisted as among the Jews; in this group, the probable number of living cases may well be, as the writer found it in certain neighborhoods of New York City, as high as eight remaining living or clinical cases to each death annually.

In the United States, the survey, previously mentioned, by the National Tuberculosis Association for the year 1940 showed that in 48 States and the District of Columbia a total of 108,555 new cases of tuberculosis were registered. But this figure, however, did not cover the total old and new cases existing in the entire country at the same time. Thus, for instance, in New York City, while in 1942, 9834 new cases were reported during the year, the Department of Health altogether handled, in both old and new registrations, the records of 31,617 pulmonary cases alone. This was in a year when the tuberculosis mortality registered locally totaled 3502.

The tuberculosis morbidity of a given community should, therefore, be computed along the lines indicated and with the qualifications noted for certain groups. In general, an average of two new living cases of clinical disease should be registered to each death annually; and, the total frank cases old and new,

in a community, may number on a given day, five for each death. (Those in contact with other cases naturally have higher morbidity rates.\*)

### MORTALITY FROM TUBERCULOSIS.

With the marked decline of tuberculosis mortality in most of the civilized or more industrialized communities lately, the present death rates are quite different from those of but a few years ago. In the United States, death rates under 100 per 100,000 population are now the rule rather than the exception. In Europe, comparatively high rates still prevail; in a few exceptional places tuberculosis mortality is still rising (for trend of tuberculosis in several countries over a period of years, see Figs. 2, 3, 4 and 5).

**Mortality, Large American Cities.**—The writer has conducted for a number of years an annual survey, based upon direct reports from local Health Commissioners, of tuberculosis mortality in the larger cities of the United States where he has taken into account—an important correction where migra-

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\*Just as among young children more are found infected when they have been in contact with other cases of tuberculosis, so are many more cases of clinical tuberculosis found in families or a household where there is already a known case than in the general population. In New York City, of 72,105 contacts, adults and children, examined at various tuberculosis clinics during the years 1930-1935, 3625 new cases were found, 3085 or 8.4 per cent among the adults and 540 or 1.5 per cent among the children—an average for the entire group of 5 per cent. In Chicago, according to records by courtesy of the Municipal Sanitarium for the years 1927, 1928, 1929 and 1935, among which 57 per cent new cases were found, the proportion there being also greater among the adults, namely, 10.4 per cent, among children it was 1.6 per cent, practically the same as in New York City. In London, the reports of the County Medical Health Officer show that in the tuberculosis dispensaries in the various metropolitan boroughs during the years from 1927-1934 inclusive, in a total of 69,733 contacts examined, 47 per cent were found tuberculous, and here too the proportion among adults was high, namely, 7.7 per cent while that among the children was 1.9 per cent. Similar and still more extensive reports are those of the examinations of contacts throughout England (except Wales and Monmouth) available by courtesy of Sir Arthur S. MacNalty, Chief Medical Officer of the Ministry of Health, for the five-year period, 1931-1935, during which 237,712 contacts were examined for the first time. Of these, 99,364 were adults and among them 9597 cases of pulmonary tuberculosis were found and 509 non-pulmonary, a ratio of 10.2 per cent with tuberculosis; among 138,348 children, there were 4176 cases of pulmonary tuberculosis, a ratio of 3 per cent, and 2453 non pulmonary cases or 1.8 per cent, a total of 4.8 per cent diagnosed tuberculous—and a grand total, therefore, of 16,735 cases of tuberculosis in the entire contact group, a ratio of 7 per cent.

Since, as the writer estimates, the present incidence of clinical cases of tuberculosis, especially in the United States, is approximately 0.5 per cent of the child population and 0.75 of the adults, it can be seen that among contacts of other cases the tuberculosis morbidity among children under fifteen years of age is nearly three times as great, for the combined group of adults and children, it is ten times that of the general population, and, among adults alone, approximately thirteen times as much as in a normal group.

It is rather striking to notice in these large and far apart communities the similarity of the findings among contacts, secondly, the much greater incidence of clinical cases of tuberculosis in the adult group. And yet the man or woman in contact in these homes is usually the partner, husband or wife, and has lived with the case certainly as long as their children. Possible factors at work must include these first, that the man or wife, among the secondary cases, has very likely been exposed to and undergone similar experiences as to housing, sufficiency or insufficiency of food and, to a certain extent, work conditions as the primary case, so that such as may have been unfavorable and hastened the development of disease in the first instance may equally have been at work upon the other partner; second, that the partner is very unlikely, though related by marriage, to be a blood or family relation to the other, but the majority of the children contacts have had a parent who already had tuberculosis. Have we here, therefore, in the latter another instance of a greater resistance to the development of acute or active disease where the parental history is positive as has already been noted by the writer and other observers (see section on inheritance)? None the less, the seriousness of contact as a source of secondary cases of tuberculosis is patent.

tion is so common as among sufferers from this disease—deaths of these city residents when they occurred in institutions, municipal, county or state, located outside the town limits. (The results are shown separately for whites and colored in Tables VI and VII and in Figs. 13 and 14.)

In 1940, 46 large cities of the United States with a total population of 32,000,000 had 18,519 tuberculosis deaths among their residents, the death rate being 58 per 100,000 population for the combined group compared, for instance,

### BRITISH ISLES

#### TREND OF MORTALITY FROM TUBERCULOSIS (ALL FORMS) SINCE 1866

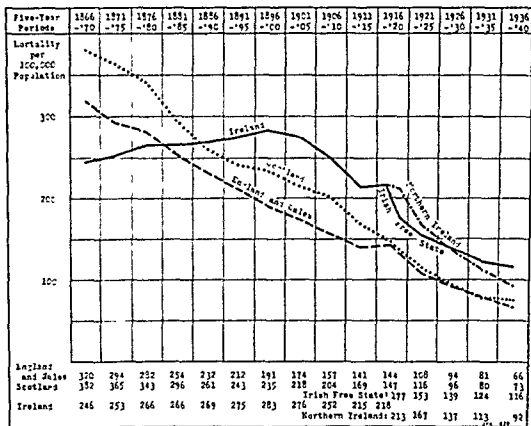


Fig. 12.

with a rate of 59 in 1939. As may be seen in Fig. 15, in only one of these 46 cities did the death rate in 1940 exceed 100 per 100,000 and in all of the remainder it ranged from 95 down to 28. Considering separately for this same group the death rates among the white and colored population in 46 of these cities with a fair-sized number of colored, the rates, of course, are markedly low for the whites and still high for the colored.

In five of the largest cities, with populations of more than a million, the resident death rates in 1940 for all racial groups averaged as follows: Los Angeles, 50; Detroit, 51; New York City, 54; Chicago, 61; and Philadelphia, 65. In nine cities, with populations ranging between 500,000 and 1,000,000, the tuberculosis death

TABLE VI

WHITE AND NONWHITE TUBERCULOSIS MORTALITY OF 46 AMERICAN CITIES IN 1940  
including their residents dying out of town

Cities	Population, July 1, 1940†			Tuberculosis Deaths†			Death Rate**		
	White	Non-white*	Total	White	Non-Wh*	All Races	Wh.	N. Wh.*	All Races
New York City	6,986,331	481,778	7,468,109	2996	1059	4055	43	220	54
Chicago	3,114,836	282,481	3,397,317	1395	689	2084	45	244	61
Philadelphia	1,678,133	252,710	1,930,843	750	508	1258	45	201	65
Detroit	1,473,633	151,189	1,624,822	530	294	824	36	194	51
Los Angeles	1,414,120	96,813	1,510,933	634	123	757	45	127	50
Cleveland	792,785	84,999	877,784	347	166	513	44	195	58
Baltimore	693,292	167,164	860,456	393	423	816	57	253	95
St. Louis	705,956	109,944	815,900	245	216	461	35	196	57
Boston	745,827	24,730	770,557	459	50	509	62	202	66
Pittsburgh	608,462	63,243	671,705	245	120	365	40	190	54
Washington, D C	476,768	190,729	667,497	183	416	599	38	218	90
San Francisco	602,388	32,152	634,540	347	79	426	58	246	67
Milwaukee	578,362	9,341	587,703	187	17	204	32	182	35
Buffalo	557,844	18,128	575,972	230	40	270	41	221	47
New Orleans	345,797	149,634	495,431	211	191	402	61	128	81
Minneapolis	487,674	5,396	493,070	137	6	143	28	111	29
Cincinnati	399,563	56,158	455,721	168	142	310	42	253	68
Newark	383,082	46,364	429,446	163	140	303	43	302	71
Kansas City, Mo.	357,231	41,933	399,164	134	69	203	38	165	51
Indianapolis	336,598	50,944	387,542	150	103	253	45	202	65
Houston	300,091	86,727	386,818	163	101	264	54	116	68
Seattle	353,963	14,407	368,370	115	35	150	32	243	41
Rochester, N. Y.	321,493	3,403	324,896	112	2	114	35	59	35
Denver	314,349	8,927	323,276	128	17	145	41	190	45
Louisville	272,456	46,904	319,360	118	87	205	43	185	64
Columbus	271,166	35,309	306,475	103	69	172	38	195	56
Portland, Ore	299,367	6,116	305,483	101	9	110	34	147	36
Atlanta	198,581	104,505	303,086	60	207	267	30	198	88
Oakland, Cal	288,220	14,396	302,616	122	14	136	42	97	45
Jersey City	287,023	13,761	300,784	135	35	170	47	254	57
Dallas, Tex	245,362	50,228	295,590	102	63	165	42	125	56
Memphis	172,324	121,613	293,937	67	174	241	39	143	82
St. Paul	283,996	4,143	288,139	76	4	80	27	97	28
Toledo	267,090	15,050	282,140	168	44	212	63	292	75
Birmingham	159,097	108,684	267,781	40	154	194	25	142	72
San Antonio	234,044	20,368	254,412	350	17	367	150	83	144
Providence	246,602	6,915	253,517	90	8	98	36	116	39
Akron	232,508	12,027	244,535	62	18	80	27	150	33
Omaha	211,669	12,421	224,090	80	16	96	38	129	43
Dayton	190,645	20,316	210,961	64	39	103	34	192	49
Syracuse	203,464	2,419	205,883	72	4	76	35	165	37
Oklahoma City	185,040	19,860	204,900	85	24	109	46	121	53
Worcester	191,654	2,000	193,654	57	4	61	30	200	32
Springfield, Mass	146,334	3,211	149,545	39	4	43	27	125	29
Paterson	135,348	4,337	139,685	47	9	56	35	208	40
Kansas City, Kan	100,487	20,961	121,448	35	15	50	35	72	41
Total	28,851,055	3,074,838	31,925,893	12495	6024	18519	43	196	58

\* Includes a small number of "other colored" than Negro \*\*Per 100,000 population. † Net mortality excludes deaths of non-residents and includes known out-of-town deaths of residents.

† Based on local estimates Compiled from preliminary reports by courtesy of municipal, state, sanatorium and other authorities

rates ran as follows: Milwaukee, 35, Buffalo, 47, Pittsburgh, 54; St. Louis, 57; Cleveland, 58; Boston, 66; San Francisco, 67, Washington, 90; Baltimore, 95.

Or again, in 46 cities, considering the tuberculosis death rate in the white population, 11 had death rates under 35, namely, Birmingham, Akron, St. Paul, Spring-



field, Minneapolis, Worcester, Atlanta, Milwaukee, Seattle, Dayton, and Portland, Ore.; 12 had rates from 35 to 40: St. Louis, Paterson, both sections of Kansas City, Rochester, N. Y., Syracuse, Detroit, Providence, Omaha, Columbus, Washington and Memphis.

In the same survey of 1940, the death rates in the colored population ranged from 59 in Rochester, N. Y., to 302 in Newark. But, as against only one city with a death rate in the white population above 100, there were but five cities where the colored death rate was under 100 per 100,000 (see Fig. 14).

One obvious factor in the tuberculosis mortality of these large cities is, of course, the proportion of the colored population (see Table VI for details by cities). In the 46 surveyed, there was a colored population of 3,074,838, and though this group was only 11 per cent of the total it suffered 33 per cent of the entire mortality, the proportion varying, of course, in different communities. In 11 cities with non-white populations exceeding 100,000 in 1940, the percentage of colored tuberculosis deaths to the total was as follows: New York City, 26 per cent; Chicago, 33 per cent; Detroit, 36 per cent; Philadelphia, 40 per cent; St. Louis, 47 per cent; New Orleans, 48 per cent; Baltimore, 52 per cent; Washington, 69 per cent; Memphis, 72 per cent; Atlanta, 78 per cent; Birmingham, 79 per cent.

TABLE VII

PROPORTION OF NEGRO TUBERCULOSIS MORTALITY IN 46 LARGE AMERICAN CITIES DURING 1940

Cities	Deaths, 1940*			Per Cent Negro	Cities	Deaths, 1940*			Per Cent Negro
	Negro	White†	Total			Negro	White†	Total	
New York City	999	3056	4055	25%	Louisville	87	118	205	42%
Chicago	673	1411	2084	32%	Columbus	69	103	172	40%
Philadelphia	503	755	1258	40%	Portland, Ore.	4	106	110	4%
Detroit	294	530	824	36%	Atlanta	207	60	267	78%
Los Angeles	92	665	757	12%	Oakland	9	127	136	7%
Cleveland	166	347	513	32%	Jersey City	35	135	170	21%
Baltimore	421	395	816	52%	Dallas	63	102	165	38%
St. Louis	216	245	461	47%	Memphis	174	67	241	72%
Boston	41	468	509	8%	St. Paul	4	76	80	5%
Pittsburgh	117	248	365	32%	Toledo	44	168	212	21%
Washington, D.C.	414	185	599	69%	Birmingham	134	40	194	79%
San Francisco	13	413	426	3%	San Antonio	17	350	367	5%
Milwaukee	17	187	204	8%	Providence	8	90	98	8%
Buffalo	39	231	270	14%	Akron	18	62	80	22%
New Orleans	191	211	402	48%	Omaha	16	80	96	17%
Minneapolis	4	139	143	3%	Dayton	39	64	103	38%
Cincinnati	142	168	310	46%	Syracuse	4	72	76	5%
Newark	138	165	303	46%	Oklahoma City	23	86	109	21%
Kansas City, Mo.	69	134	203	34%	Worcester	3	58	61	5%
Indianapolis	103	150	253	41%	Springfield, Mass.	4	39	43	9%
Houston	101	163	264	38%	Paterson	9	47	56	16%
Seattle	10	140	150	7%	Kansas City, Kan.	15	35	50	30%
Rochester	2	112	114	2%					
Denver	15	130	145	10%	Total, 46 Cities..	5786	12733	18519	31.2%

\* Net mortality: excludes deaths of non-residents and includes known out-of-town deaths of city residents. † Includes a small number of "other colored" than Negro.

Compiled from preliminary reports by courtesy of municipal, state, sanatorium and other authorities.

**TUBERCULOSIS DEATH RATE  
IN 46 LARGE AMERICAN CITIES  
AMONG WHITE RESIDENTS,\* YEAR 1940**

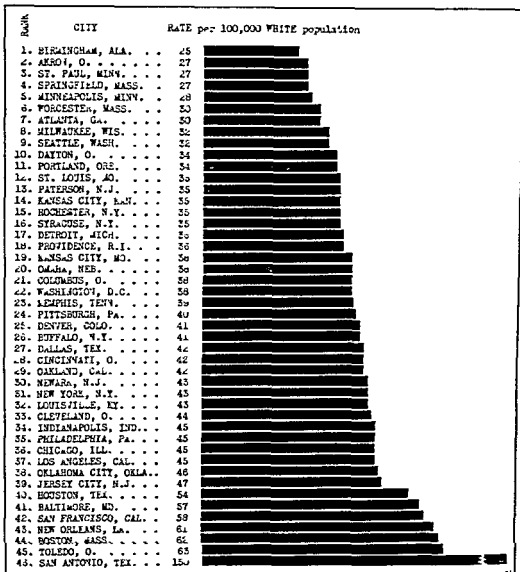


Fig. 13.

\*Based on net mortality only namely, excludes non-residents and includes known out-of-town deaths of city residents—residence being defined according to local practice

**By States.**—The geographic distribution of mortality in various States is shown in Fig. 16 for the year 1942. While it is correct that the highest mortality rates are found in certain southwestern States like Nevada, New Mexico, Arizona and Texas, it should at once be recalled that these sections are likewise the ones sought by health seekers and that the deaths taking place there represent both those of residents and non-residents visiting there. Secondly, high rates are also found in southern States as in Tennessee, and in Kentucky and Virginia where a large proportion of the population is colored. But, after excluding health resort communities and considering only the mortality among the whites, the

**NEGRO TUBERCULOSIS DEATH RATE**  
**IN 46 LARGE AMERICAN CITIES**  
**YEAR 1940**

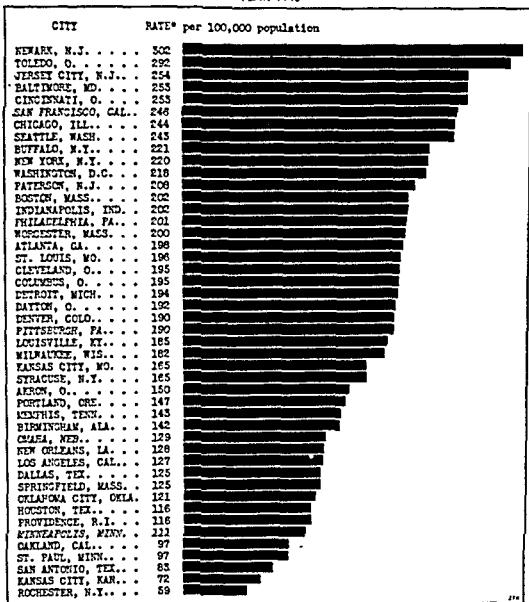


Fig. 14.

\*Based on net mortality only, namely, excludes non-residents and includes known out-of-town deaths of city residents—residence being defined according to local practice.

Compiled from preliminary reports by courtesy of municipal, state, sanatorium and other authorities.

highest death rate is still found in Maryland, Kentucky and Tennessee (see Table IX for separate rates in certain States among the white and colored).\*

In 1942, only one State had a death rate above 75 per 100,000 population,

\*For additional data as to mortality in certain other cities of the United States, particularly those with a large proportion of colored, the reader is referred to the Mortality Statistics of the United States Bureau of the Census.

TABLE VIII

NET TUBERCULOSIS MORTALITY OF RESIDENTS OF 46 LARGE AMERICAN CITIES\*  
DURING 1939 AND 1940

Cities ‡	Population July 1, 1940	RESIDENT MORTALITY Only, Anywhere						
		Number of Deaths, 1940			1939 Total† Deaths	Death Rate per 100,000		Change in 1940 Rate
		In Town	Out of Town†	Total		1940	1939	
New York City . . .	7,468,109	3,548	507	4,055	4,234	54	57	- 5%
Chicago . . .	3,397,317	1,857	227	2,084	2,103	61	62	- 2%
Philadelphia . . .	1,930,843	1,150	108	1,258	1,198	65	62	+ 5%
Detroit . . .	1,624,822	638	186	824	937	51	58	-12%
Los Angeles . . .	1,510,933	619	138	757	803	50	54	- 7%
Cleveland . . .	877,784	424	89	513	547	58	62	- 6%
Baltimore . . .	860,456	559	257	816	673	95	79	+20%
St. Louis . . .	815,900	309	152	461	441	57	54	+ 6%
Boston . . .	770,557	413	96	509	469	66	61	+ 8%
Pittsburgh . . .	671,705	303	62	365	377	54	56	- 4%
Washington, D. C	667,497	384	215	599	551	90	85	+ 6%
San Francisco . .	634,540	383	43	426	409	67	64	+ 5%
Milwaukee . . .	587,703	74	130	204	237	35	40	-13%
Buffalo . . .	575,972	219	51	270	310	47	54	-13%
New Orleans . . .	495,431	394	8	402	380	81	77	+ 5%
Minneapolis . . .	493,070	51	92	143	149	29	30	- 3%
Cincinnati . . .	455,721	296	14	310	257	68	56	+21%
Newark . . .	429,446	149	154	303	273	71	63	+13%
Kansas City, Mo.	399,164	196	7	203	206	51	52	- 2%
Indianapolis . . .	387,542	218	35	253	244	65	63	+ 3%
Houston . . .	386,818	259	5	264	251	68	66	+ 3%
Seattle . . .	368,370	122	28	150	168	41	46	-11%
Rochester . . .	324,896	42	72	114	108	35	33	+ 6%
Denver . . .	323,276	127	18	145	161	45	50	-10%
Louisville . . .	319,360	113	92	205	192	64	60	+ 7%
Columbus . . .	306,475	95	77	172	169	56	55	+ 2%
Portland, Ore . .	305,483	61	49	110	126	36	41	-12%
Atlanta . . .	303,086	200	67	267	292	88	97	- 9%
Oakland, Cal. . .	302,616	51	85	136	134	45	45	0%
Jersey City . . .	300,784	162	8	170	167	57	55	+ 4%
Dallas, Tex. . .	295,590	96	69	165	178	56	61	- 8%
Memphis . . .	293,937	191	50	241	296	82	102	-20%
St. Paul . . .	288,139	66	14	80	88	28	31	-10%
Toledo . . .	282,140	202	10	212	190	75	67	+12%
Birmingham . . .	267,781	172	22	194	211	72	79	- 9%
San Antonio . . .	254,412	316	51	367	385	144	153	- 6%
Providence . . .	253,517	55	43	98	114	39	45	-13%
Akron . . .	244,535	61	19	80	64	33	26	+27%
Omaha . . .	224,090	78	18	96	74	43	33	+30%
Dayton . . .	210,961	59	44	103	114	49	54	- 9%
Syracuse . . .	205,883	28	48	76	84	37	41	-10%
Oklahoma City . .	204,900	79	30	109	112	53	55	- 4%
Worcester . . .	193,654	51	10	61	69	32	36	-11%
Springfield, Mass	149,545	31	12	43	47	29	31	- 6%
Paterson . . .	139,685	16	40	56	61	40	44	- 9%
Kansas City, Kan	121,448	38	12	50	47	41	39	+ 5%
Total . . .	31,925,893	14,955	3,564	18,519	18,700	58.0	58.8	- 2%

\* Excludes deaths of non-residents and includes known out-of-town deaths of city residents—residence being defined according to local practice. † Includes known deaths of city residents occurring in out-of-town institutions or health resorts. ‡ San Diego not included owing to difficulty of ascertaining residence.

Compiled from preliminary reports by courtesy of municipal, state, sanatorium and other authorities.

## TUBERCULOSIS DEATH RATE

46 LARGE AMERICAN CITIES

YEAR 1940

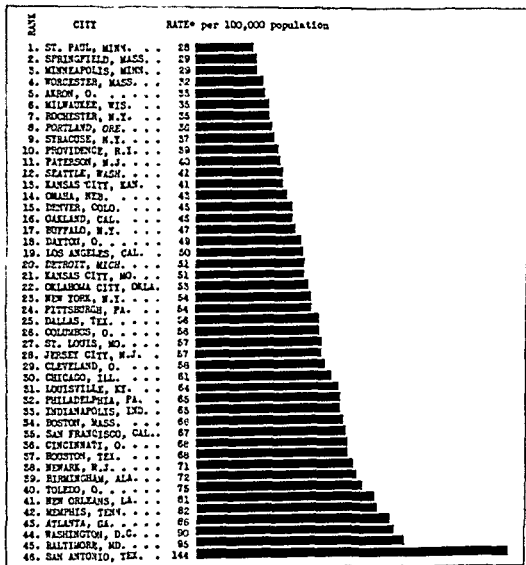


Fig. 15.

\*Based on net mortality only, namely, excludes non-residents and includes known out-of-town deaths of city residents—residence being defined according to local practice.

namely, Arizona; four had rates between 60 and 75, New Mexico, Kentucky, Maryland and Tennessee. There were 16 States with rates ranging between 35 and as low as 12: Connecticut, 34; Michigan, 33; Vermont, 31; Maine, 30; South Dakota, 28; Oregon, 28; Kansas, 26; Minnesota, 26; Wisconsin, 24; New Hampshire, 23; North Dakota, 20; Idaho, 18; Iowa, 17; Wyoming, 16; Nebraska, 14; Utah, 12.

**Mortality in Foreign Cities.**—In various cities outside the United States, except, perhaps, in Australia, New Zealand and South Africa, tuberculosis

TABLE IX  
TUBERCULOSIS DEATH RATE\* BY COLOR IN ELEVEN STATES†  
Years 1920, 1925, 1930, 1935 and 1940

State	1940‡	1935	1930	1925	1920	State	1940‡	1935	1930	1925	1920
Alabama						Mississippi:					
White	31	37	49	58	.	White.....	24	29	39	45	48
Colored	94	110	151	168	.	Colored..	74	83	138	154	199
Florida						No. Carolina:					
White	28	34	42	50	68	White... .	26	35	50	67	82
Colored	112	108	134	146	180	Colored..	110	113	146	167	194
Georgia						So. Carolina:					
White	27	34	42		‡56	White ....	21	25	36	44	65
Colored	90	103	134		‡141	Colored ..	82	92	128	156	174
Kentucky.						Tennessee:					
White	62	66	84	105	130	White . .	59	70	89	102	130
Colored	162	162	234	256	365	Colored .	149	169	257	268	313
Louisiana.						Virginia:					
White	38	40	53	63	81	White .	37	49	60	75	94
Colored	95	116	138	180	234	Colored.	124	152	180	206	255
Maryland:											
White	48	52	67	88	110						
Colored	238	210	255	286	325						

\* Per 100,000 population † Mostly southern, or with large Negro population. ‡ Year 1922.  
‡ Based on April 1st enumerated population  
Compiled from reports, United States Bureau of the Census.

death rates are generally high (for 175 great cities throughout the world see Table X). In Europe, according to the reports of the Health Section of the League of Nations, cities with a tuberculosis mortality rate in 1935 under 100 per 100,000 included Birmingham, Bristol, Edinburgh, Kingston, Leeds, London, Sheffield, Antwerp, Brussels, Ghent, Liege, Amsterdam, Rotterdam, The Hague, Utrecht, Basle, Berne, Zurich, Bergen, Oslo, Gothenberg, Malmö, Berlin, Breslau, Cologne, Dresden, Essen, Frankfurt, Hamburg, Königsberg, Leipzig, Munich, Nuremberg, Bratislava, Moravska-Ost., Plzen, Lyons and Barcelona (see Table X).

Among cities of Europe with death rates still above 200 per 100,000 population were noted Lisbon, Oporto, Nancy, Nantes, Reims, Rouen, Athens, Piraeus, Salonika, Istanbul, Bucharest, Cernauti, Chisinau and Galati.

In Africa, death rates are comparatively low in Egypt and among Europeans in the South Union but reach 158 in Algiers and 246 in Tunis.

In Central or South America, with much colored or Indian admixture, tuberculosis death rates are high, especially in the cities: 211 in Montevideo, 230 in Santa Fe, 233 in Belem, 244 in Panama, 289 in Manaus, 296 in Rio de Janeiro, 303 in Recife, 341 in Maracaibo, 343 in Guatemala, 361 in San Salvador, 413 in Caracas, 465 in Lima, and 578 in Callao.

In Asia, reports can only cover certain limited sections or communities where there is some degree of medical service and certification of causes of death. In 1935, while Jerusalem had a tuberculosis mortality of only 48 per 100,000 population, rates above two hundred were known to prevail in the following places: Colombo, 208; Nagoya, 216; Tokio, 220; Calcutta, 224; Rangoon, 225; Singapore, 230; Osaka, 236; Bagdad, 239; Izmir, 246; Delhi, 246; Nagasaki, 264;

## TUBERCULOSIS MORTALITY, UNITED STATES, YEAR 1942

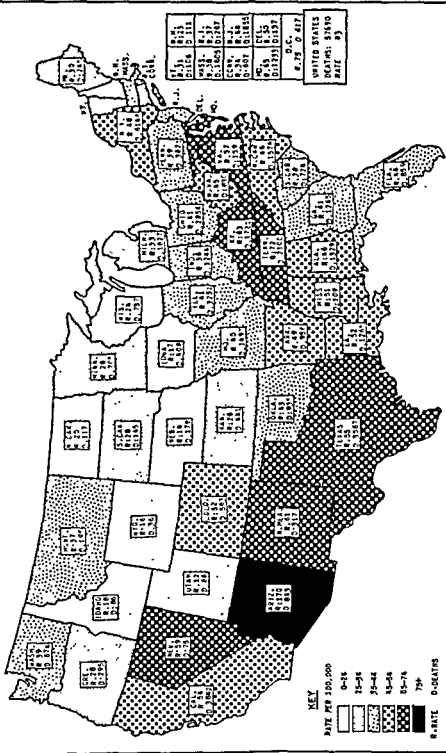
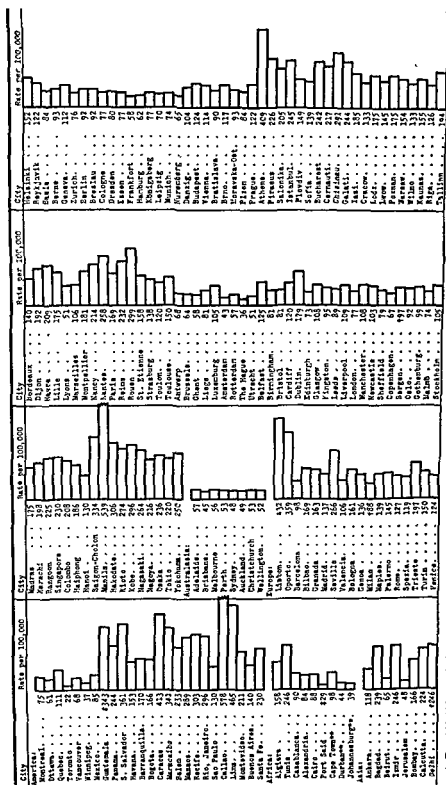


Fig. 16.  
From preliminary reports by courtesy of state departments of health and  
the National Tuberculosis Association

TABLE X  
TUBERCULOSIS DEATH RATE\* IN 175 GREAT CITIES OF THE WORLD, IN 1935



\* Per 100,000 population. \*\* European population only. † Year 1934. ‡ Tuberculosis of the respiratory system.

Note: For cities of the United States see Fig. 15.

From Statistics of Notifiable Diseases, Health Section, League of Nations.

Whenever possible, the data refer to the resident population.



Yokohama, 250; Kioto, 274; Kobe, 296; Hakodate, 306; Saigon-Cholon, 334; and Manila, 539. Everywhere tuberculosis is taking a daily toll of human lives!

**Mortality, by Countries.**—Mortality rates during a recent year are shown in Fig. 17 for 53 countries. Comparatively low rates may be noted in New Zealand, among the white population in South Africa, in Australia, the United States, Denmark, Curacao, Colombia, Salvador and the Netherlands. Death rates above 150 per 100,000 population were still recorded recently in Bulgaria, Portugal, Estonia, Roumania, Finland, Newfoundland, Japan, Puerto Rico, Chile and Alaska.

### FORMS OF TUBERCULOSIS.

The differentiation in morbidity or mortality records of tuberculosis into the pulmonary type, that affecting the respiratory system, and the non-pulmonary, that of other parts of the body, has the advantage of indicating roughly, especially during the earlier period of life, where most of the bovine infection has occurred. In the United States (see Table XII), of 60,428 deaths charged to tuberculosis during 1940, 55,576 or 92 per cent were recorded as having been of the pulmonary type and 4,852 of other forms of tuberculosis: meningeal, intestinal, vertebral, and so forth. In England and Wales, where there is a greater amount of bovine infection, the same year in a total of 28,144 tuberculosis deaths 4,484 or 16 per cent were said to be non-pulmonary; in Scotland, during the year 1936, the proportion rose to 25 per cent.

The present comparatively low rate of non-pulmonary forms of tuberculosis in the United States would seem to have followed largely the adoption of measures for the control of bovine tuberculosis, especially the limitation of infected milk by pasteurization. In New York City, the death rate from non-pulmonary forms of tuberculosis prior to the adoption of measures for the general pasteurization of milk around 1915 was 9 times what it is now. Also important towards that achievement has been the increasing segregation in hospitals of advanced cases and the removal therefore of these dangerous sources of infection from intimate contact with children.

TABLE XI  
TUBERCULOSIS DEATH RATE\* IN TWENTY LARGE CITIES OF THE WORLD  
Years 1910, 1915, 1920, 1925, 1930 and 1935

Cities	1910	1915	1920	1925	1930	1935	Cities	1910	1915	1920	1925	1930	1935
New York City	211	196	126	87	73	60	Melbourne...	121	94	98	74	167	56
London....	165	199	129	112	99	77	Budapest....	355	397	448	292	224	112
Berlin....	209	207	176	135	101	92	Rome....	254	241	238	232	143	127
Chicago.....	178	171	97	81	66	56	Prague....	367	338	253	174	151	122
Paris.....	411	376	272	283	231	169	Madrid....	290	327	392	259	204	137
Vienna.....	298	405	196	161	114	114	Amsterdam..	168	152	157	96	72	43
Rio de Janeiro..	404	434	393	294	272	296	Copenhagen..	149	143	118	105	189	67
Sydney....	89	62	171	153	151	48	Stockholm...	287	273	209	163	143	105
Warsaw....	300	410	337	229	210	154	Edinburgh...	170	162	134	134	99	73
Sao Paulo....	151	126	110	107	101	130	Oslo.....	236	214	209	169	147	92

\* Per 100,000 population. † Rates include deaths of residents in institutions outside metropolis.  
‡ Based on resident or domiciled population. § Average annual rate, years 1911-13, for Vienna; year 1912, for Warsaw and Madrid.

# TUBERCULOSIS DEATH RATE IN FIFTY-THREE DIFFERENT COUNTRIES

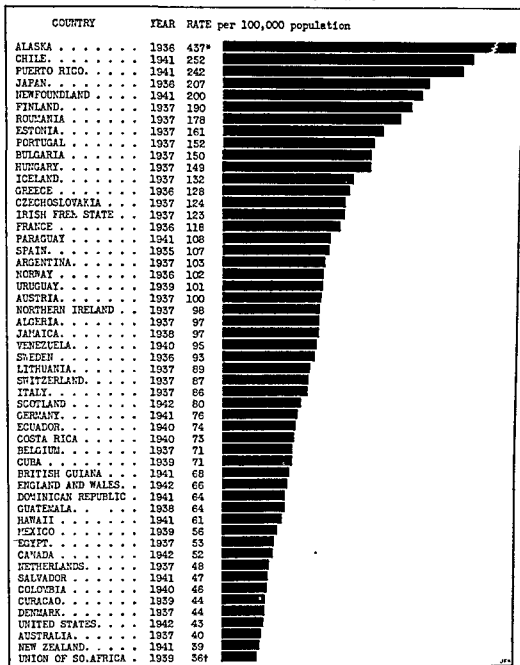


Fig 17.

Based on data by courtesy of statistical service, National Tuberculosis Association.

\*White and Indian † White population only.

Of the non-pulmonary tuberculosis deaths in the United States, one-fourth approximately involve the meninges; one-fifth, the intestines and peritoneum; one-tenth only, the vertebral column; tuberculosis of the joints and of other organs furnish nowadays even lesser fractions of mortality. These, of course, are divi-

TABLE XII

TUBERCULOSIS MORTALITY, PULMONARY AND OTHER FORMS, BY STATES, YEAR 1940

State	Population 1940*	Number of Deaths *					Rate per 100,000		
		All Forms	Pul-monary	Per Cent	Other Forms	Per Cent	All Forms	Pul-monary	Other Forms
United States	131,970,224	60,428	55,576	92	4,852	8	45.8	42.1	3.7
Alabama	2,832,961	1,503	1,383	92	120	8	53.1	48.8	4.3
Arizona	499,261	713	674	95	39	5	142.8	135.0	7.8
Arkansas	1,949,387	1,020	985	97	35	3	52.3	50.5	1.8
California	6,907,387	3,879	3,541	91	338	9	56.2	51.3	4.9
Colorado	1,123,296	500	458	92	42	8	44.5	40.8	3.7
Connecticut	1,709,242	619	561	91	55	9	36.2	33.0	3.2
Delaware	266,505	134	120	90	14	10	50.3	45.0	5.3
Dist. Columbia	677,000	569	503	88	66	12	84.0	74.3	9.7
Florida	1,897,414	969	918	95	51	5	51.1	48.4	2.7
Georgia	3,123,723	1,562	1,448	93	114	7	50.0	46.4	3.6
Idaho	524,873	96	75	78	21	22	18.3	14.3	4.0
Illinois	7,897,241	3,732	3,439	92	293	8	47.3	43.6	3.7
Indiana	3,427,796	1,402	1,258	90	144	10	40.9	36.7	4.2
Iowa	2,538,268	446	399	89	47	11	17.6	15.7	1.9
Kansas	1,801,028	450	414	92	36	8	25.0	23.0	2.0
Kentucky	2,845,627	1,954	1,767	90	187	10	68.7	62.1	6.6
Louisiana	2,363,880	1,381	1,318	95	63	5	58.4	55.7	2.7
Maine	847,226	260	229	88	31	12	30.7	27.0	3.7
Maryland	1,821,244	1,326	1,230	93	96	7	72.8	67.5	5.3
Massachusetts	4,316,721	1,601	1,495	93	106	7	37.1	34.6	2.5
Michigan	5,256,106	1,794	1,583	88	211	12	34.1	30.1	4.0
Minnesota	2,792,300	746	681	91	65	9	26.7	24.4	2.3
Mississippi	2,181,796	1,091	1,015	93	76	7	50.0	46.5	3.5
Missouri	3,784,664	1,759	1,647	94	112	6	46.5	43.5	3.0
Montana	559,456	231	202	87	29	13	41.3	36.1	5.2
Nebraska	1,315,834	230	204	89	26	11	17.5	15.5	2.0
Nevada	110,247	78	70	90	8	10	70.8	63.5	7.3
New Hampshire	491,524	113	101	89	12	11	23.0	20.6	2.4
New Jersey	4,160,165	1,849	1,714	93	135	7	44.4	41.2	3.2
New Mexico	531,818	355	322	91	33	9	66.8	60.6	6.2
New York	13,479,142	6,166	5,651	92	515	8	45.7	41.9	3.8
North Carolina	3,571,623	1,608	1,492	93	116	7	45.0	41.8	3.2
North Dakota	641,935	125	106	85	19	15	19.5	16.5	3.0
Ohio	6,907,612	2,829	2,569	91	260	9	41.0	37.2	3.8
Oklahoma	2,336,434	1,148	1,071	93	77	7	49.1	45.8	3.3
Oregon	1,089,684	308	275	89	33	11	28.3	25.3	3.0
Pennsylvania	9,900,180	4,252	3,948	93	304	7	42.9	39.9	3.0
Rhode Island	713,346	246	227	92	19	8	34.5	31.8	2.7
South Carolina	1,899,804	912	851	93	61	7	48.0	44.8	3.2
South Dakota	642,961	200	179	90	21	10	31.1	27.8	3.3
Tennessee	2,915,841	2,211	2,020	91	191	9	75.8	69.3	6.5
Texas	6,414,824	3,815	3,571	94	244	6	59.5	55.7	3.8
Utah	550,310	94	81	86	13	14	17.1	14.7	2.4
Vermont	359,231	156	145	93	11	7	43.4	40.4	3.0
Virginia	2,677,773	1,574	1,424	90	150	10	58.8	53.2	5.6
Washington	1,736,191	692	633	91	59	9	39.9	36.5	3.4
West Virginia	1,901,974	882	807	91	75	9	46.4	42.4	4.0
Wisconsin	3,137,587	803	730	91	73	9	25.6	23.3	2.3
Wyoming	250,742	45	39	87	6	13	17.9	15.5	2.4

\* By place of residence. † Populations for 1940 are those enumerated in the Federal census of April 1, 1940, except for the United States and the District of Columbia which are estimates as of July 1. Based on reports U. S. Bureau of the Census.

sions based upon the outstanding terminal condition at death; on the other hand, Lawrason Brown estimated that intestinal tuberculosis complicates the great majority of all cases of pulmonary tuberculosis.

The proportion of the non-pulmonary forms of tuberculosis still varies greatly in different sections of the United States. While, as noted, such types of the disease cause approximately one death to twelve from pulmonary tuberculosis, a higher proportion is still found especially in comparatively rural sections or states.

States where the non-pulmonary forms of tuberculosis caused from 12 to 15 per cent of all the deaths from this disease in 1940 were North Dakota, Michigan, Maine, Montana, Utah and Wyoming; one in which so-called surgical forms of tuberculosis exceeded 15 per cent was Idaho. In other words, in certain sections of the United States, non-pulmonary forms of tuberculosis may be responsible for anywhere from one-eighth to one-fifth of all the deaths from this disease.

The various forms of tuberculosis, as well known, vary according to age. Among children under 5 years of age in the United States during 1940, 36 per cent of the entire tuberculosis mortality was of the meningeal type, 43 per cent of the respiratory system, one-sixth was disseminated and one-fiftieth intestinal. Among those 5 to 10 years of age, tuberculosis of the respiratory system was responsible for 49 per cent of the deaths, meningeal 31 per cent, and intestinal 2 per cent; among those 10 to 15, tuberculosis of the respiratory system prevailed in 75 per cent, meningeal in 12 per cent, and intestinal in 4 per cent; among adults, 25 to 35 years of age, the proportion of deaths due to tuberculosis of the respiratory system was 94 per cent.

As already noted, in England and Wales, non-pulmonary forms of tuberculosis were said to prevail in 16 per cent of the deaths registered in 1940. A wide variation as to forms of tuberculosis is reported in a number of cities of the world. For the two-year period 1935-36, for instance, the non-pulmonary type of tuberculosis was held responsible in Rio de Janeiro for 4 per cent of all the tuberculosis deaths; in Berlin, 7 per cent; in Sidney, 8 per cent; in London, 11 per cent; in Bombay, 13 per cent; in Oslo, Copenhagen, Paris and Madras, 14 per cent; in Montreal, 16 per cent; in Edinburgh, 20 per cent; in Tokio, 25 per cent.

#### FACTORS INFLUENCING MORTALITY.

While surveys of the incidence of tuberculous infection do not reveal significant differences on the mere score of sex or racial origin, the actual mortality of these groups is quite different at certain times of life or in certain places.

**Sex.**—Of the 60,428 deaths from tuberculosis in the United States in 1940, 35,795 were of the male sex and 24,633 of the female sex (see Table XIII and Fig. 18), the death rate being 54 for the former and 38 for the latter. In other words, on an average that year the male death rate exceeded the female by nearly 42 per cent; in New York City, the male rate, 65, was 97 per cent higher than the female, which was only 33. This difference between the two sexes varies with age; until they are 10 years old the tuberculosis mortality of boys exceeds that of girls, but between the ages of 10 and 30 the female death rate is strikingly

## TUBERCULOSIS DEATHS BY SEX AND AGE

UNITED STATES, 1940

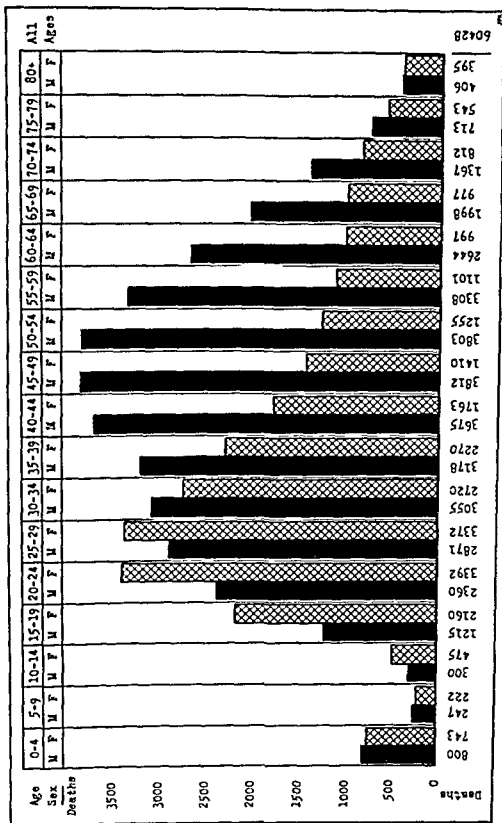


Fig. 18.

Based upon reports, U. S. Bureau of the Census.

TABLE XIII  
TUBERCULOSIS MORTALITY BY SEX AND AGE  
United States, Year 1940

Ages	Number of Deaths			Rate per 100,000*		
	Total	Male	Female	Both Sexes	Male	Female
All Ages	60,428	35,795	24,633	46	54	38
0- 5	1,543	800	743	15	15	14
5- 9	469	247	222	4	5	4
10-14	775	300	475	7	5	8
15-19	3,375	1,215	2,160	27	20	35
20-24	5,752	2,360	3,392	50	41	58
25-29	6,243	2,871	3,372	56	53	60
30-34	5,775	3,055	2,720	56	60	53
35-39	5,448	3,178	2,270	57	67	47
40-44	5,438	3,675	1,763	62	83	40
45-49	5,222	3,812	1,410	63	91	35
50-54	5,058	3,803	1,255	70	101	36
55-59	4,409	3,308	1,101	75	110	39
60-64	3,641	2,644	997	77	110	43
65-69	2,975	1,998	977	78	105	51
70-74	2,179	1,367	812	85	108	63
75+	2,057	1,119	938	78	90	67

\* Enumerated population, April 1, 1940

Note Total includes 43 male, 26 female or 69 deaths "age unknown."

Based on reports U S Bureau of the Census.

TUBERCULOSIS DEATH RATE  
AMONG WHITE AND COLORED POPULATION  
UNITED STATES, 1940

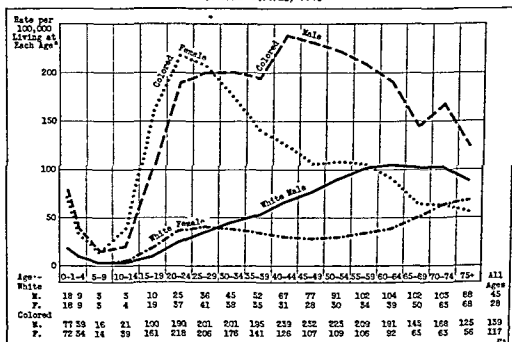


Fig. 19

Based upon reports, U S Bureau of the Census.

\*As enumerated April 1, 1940.

**FEMALE TUBERCULOSIS DEATH RATE BY AGE**  
**YEARS 1900, 1910, 1920, 1930, 1940**  
**UNITED STATES (EXPANDING) DEATH REGISTRATION AREA**

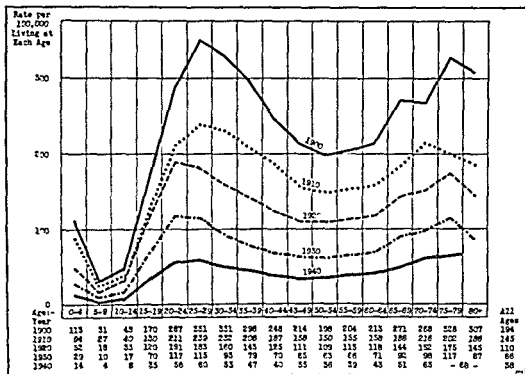


Fig. 20.

Based on reports by U. S. Census Bureau, through courtesy Statistical Service, National Tuberculosis Association.

higher; after age 30, in the United States, the male tuberculosis mortality exceeds throughout the remainder of life that of the female, the difference being particularly great between the ages of 35 and 70.

This excess of the male tuberculosis death rate over that of the female is somewhat typical in urbanized or industrialized communities; the same situation is noted for instance in England and Wales. There are several exceptions, however, namely, in Italy where the female death rate exceeds, especially through the child-bearing period; in the Netherlands, the female tuberculosis death rate exceeds that of the males up to age 40. Other countries, where the female rate exceeds that of the males, might be noted: Denmark, Japan, both sections of Ireland, the Netherlands, Norway, Sweden.

The differences in the mortality rates between the two sexes in the same communities suggest that here we have at work factors probably independent of heredity, or of food and housing conditions since both live in the same households mainly. They are very likely due, these differential mortalities, to differences in labor conditions and the burdens carried on daily by one or the other sex.

**Age.**—The factor of age is most important in influencing tuberculosis mortality (see Table XIII and Fig. 19). Until recent years in many places the tuberculosis mortality rate was really highest during the first year of life, but now the

picture has been radically altered—probably due to the more and more extensive segregation in hospitals and sanatoria of open cases of tuberculosis nowadays as well as increased home and sanitary supervision of all members of families with tuberculosis (see Figs. 20 and 21). For instance, in 1900, in the ten original registration states the tuberculosis mortality rate among male infants, under one year of age, was 350 per 100,000 living and was the highest at that time for any age group; in 1940, it was only 25 and the tuberculosis peak, 110, was now among men in the age group 55 to 65. In the female sex, in 1900, the infant tuberculosis death rate of 295 though very high was exceeded by that of young women 25 to 30; on the other hand, in 1940, the female infant death rate of 24 was one-third the highest rate, now 68, reached only among women past 75 years of age.

At present, in the United States, the lowest tuberculosis death rate, namely, 4 per 100,000 living, is among girls 5 to 10 years; among males, the lowest rate, 5, is found among boys 5 to 15 years old. The highest tuberculosis death rate among males is in the age group 55 to 65; among females, the group past 75 years now experiences the greatest tuberculosis mortality—though another peak, somewhat lower, is reached among young women 25 to 30 years of age. A few years ago Dauer and Lumsden<sup>41</sup> have brought out the rather striking characteristic of an "old-age type" of tuberculosis being prevalent in certain States of the South in

### MALE TUBERCULOSIS DEATH RATE BY AGE

YEARS 1900, 1910, 1920, 1930, 1940

UNITED STATES (EXPANDING) DEATH REGISTRATION AREA

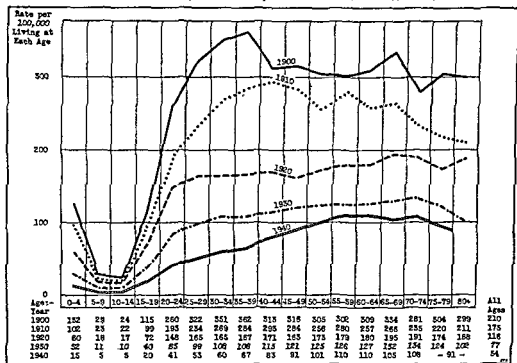


Fig. 21.

Based on reports by U. S. Census Bureau, through courtesy Statistical Service,  
National Tuberculosis Association.



the white population. Thus, for instance, in 11 southeastern States, during the period 1930-1932, among white males the highest tuberculosis rate was found in these groups: 55 to 65 years of age, 124 per 100,000 living; 65 to 75, 177; 75 and over, 203; likewise, in females of the same age the rates were, respectively, 111, 181 and 224. Among the colored, the high rates concentrated more in middle adult life. In England and Wales, the highest tuberculosis death rate among males occurs between the ages of 45 and 55; and among females, in the age group 20 to 25. In Ireland, the highest mortality rates are fairly close in both sexes among younger adults, namely, among women 20 to 25 and among men 25 to 30. In Paris, while the highest tuberculosis death rate is found among women 20 to

TABLE XIV

TUBERCULOSIS DEATH RATE BY SEX AND AGE, AMONG WHITE AND COLORED  
United States, Years 1920 and 1940 (Expanding Registration Area)

Age	Death Rate* Year 1920				Death Rate* Year 1940				Ratio, Colored to White, 1940		Rate Decline 1940 from 1920			
	White		Colored		White		Colored				White		Colored	
	M	F	M	F	M	F	M	F	M	F	M	F		
0-1	115	193	195	190	18	18	77	72	4.3	4.0	84%	81%	61%	62%
1-4	44	38	93	88	9	9	39	34	4.3	3.8	80%	76%	58%	61%
5-9	15	14	52	61	3	3	16	14	5.3	4.7	80%	79%	69%	77%
10-14	14	24	58	128	3	4	21	139	7.0	9.8	79%	83%	64%	70%
15-19	55	99	262	346	10	19	100	161	10.0	8.5	82%	81%	62%	53%
20-24	117	158	467	510	25	37	190	218	7.6	5.9	79%	77%	59%	57%
25-34	144	147	392	419	40	40	201	192	5.0	4.8	72%	73%	49%	54%
35-44	150	116	336	293	59	33	215	135	3.6	4.1	61%	72%	36%	54%
45-54	153	93	286	247	84	29	227	108	2.7	3.7	45%	69%	21%	56%
55-64	164	101	289	224	103	36	201	100	2.0	2.8	37%	64%	30%	53%
65-74	176	132	332	222	102	55	152	64	1.5	1.2	42%	58%	54%	71%
75+	151	139	266	202	88	68	125	56	1.4	0.8	42%	51%	53%	72%
All Ages	104	95	254	268	45	28	139	117	3.1	4.2	57%	71%	45%	56%

\* Per 100,000 living at each age.

Note: 1920 group of Registration States included 34 states and District of Columbia with a population of 86,079,263 (78,882,192 white, 7,197,071 colored); in 1940 population for entire continental United States was 131,669,275 (118,214,870 white, 13,454,405 colored). Tuberculosis mortality totaled, in 1920, 56,307 (41,989 white, 14,318 colored) and, in 1940, 60,428 (43,211 white, 17,217 colored). Based on reports, U. S. Bureau of the Census.

25, unusually high rates prevail among old men 60 to 65. In various countries, significant differences if any in the mortality of the two sexes are generally confined to the adult periods of life.

It should be recalled that Brownlee<sup>1</sup> thought that tuberculosis assumed three main types, namely, the "young adult type," the "middle age type" and "the old age type." In New York City at present among Negroes there might be said to prevail a young adult type of tuberculosis; similarly, among white females. On the other hand, among Jewish women in the same community a middle age type of tuberculosis prevails, and among Jewish men an old age type.

The decline of tuberculosis, especially in the United States, has been accompanied by marked changes in the rates of the two sexes especially at particular ages (see Table XIV). For instance, between 1920 and 1940, among white males



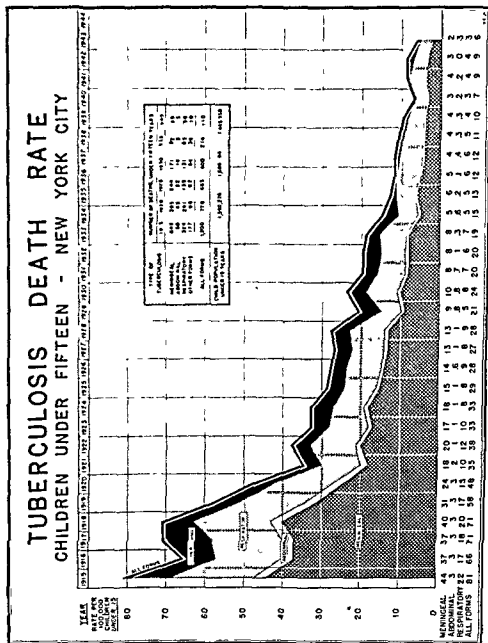


Fig. 23.

Based upon reports, Bureau of Records, Department of Health, City of New York.  
G. J. Drolet, Statistician, New York Tuberculosis and Health Association.

the death rate has declined on an average for all ages by 57 per cent, and among white females by 71 per cent. At the same time, among the colored decreases of 45 per cent in the male sex have been registered and of 56 per cent in the female. Both among the whites and the colored the decline has been especially marked among infants under one year of age as already noted, the rate having been reduced by more than three-fourths in the first group and by more than one-half in the second. On the debated question as to whether or not lately there has been some increase of mortality among young women, it should be stated that there is no evidence whatever at the present time in the United States of a higher tuberculosis rate among them now than formerly. There was indeed a tendency during the World War I period or decade 1910-1920, for the death rate of young women 15 to 20 years of age to remain somewhat stationary, namely, 133 in 1910 and 132 in 1920—in the ten original registration States—but in 1940 the rate had fallen to 35.

### PULMONARY TUBERCULOSIS DEATH RATE, UNITED STATES

#### DURING A RECENT QUARTER OF A CENTURY

Mortality of five Industrial and five Agricultural States Compared—also, of ten large Cities—through the War Period and the 1918 Influenza Epidemic

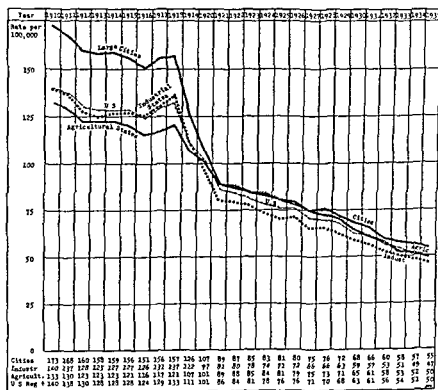


Fig. 24.

Notes Agricultural states include California, Indiana, Minnesota, North Carolina and Wisconsin, industrial states, Massachusetts, New Jersey, New York, Ohio and Pennsylvania. Ten cities New York, Chicago, Philadelphia, Detroit, Los Angeles, Cleveland, St. Louis, Baltimore, Boston and Pittsburgh. From 1910 to 1932 covers the expanding U. S. Registration Area; beginning 1933, entire Continental United States. Data based on reports, United States Bureau of the Census.

While in general, in the United States, the male tuberculosis rate is higher than that of the female sex, Dauer<sup>42</sup> has brought out interestingly that in certain sections the two tend to become equal and sometimes the first may even be lower. Thus, while the ratio of male tuberculosis deaths to female deaths in the Registration Area during the period 1931-1934 was 1.24, in comparatively rural or less industrialized sections, like Maine, it was 1.05; in Indiana, 0.97; in Iowa, 0.91; in North Dakota, 0.92; among the white population in Tennessee, 0.86. But in Pennsylvania the male ratio to the female was 1.31; in Massachusetts, 1.43; and, in New York, 1.59.

**Urbanization.**—With the greater proportion of the population of the United States now residing in towns and cities, it is difficult to measure the influence of urbanization—at least by contrast with that of comparatively sparsely settled places. Furthermore, in the so-called rural districts the problem of studying mortality is complicated by the presence there frequently of health resorts or sanatoria; again, there is the modifying factor of a different age composition of the population, youth migrating in great numbers to the cities and the very young or aged remaining in the country.

Dublin and Van Buren<sup>43</sup> remark, however, that in 1910 in 20 states the urban tuberculosis death rate exceeded the rural in every instance but one, whereas in 1925 in twelve the urban rate was lower. In cities, especially, sanitary improvements have made great progress and there has been perhaps more active organization of antituberculosis work, milk pasteurization, a cleaner water supply, closer inspection of food, which have all affected favorably the urban rate (see Fig. 24 comparing death rates in industrial and agricultural States during the 25-year period 1910-1935).

Probably a fairer test of the influence of urbanization is to compare the tuberculosis death rates of obviously industrial states with those of agricultural sections. For instance, in 1940, the death rate for New York State, 46 per 100,000 population, was 2.7 times that of Iowa, which was only 17; the highly industrialized State of Pennsylvania, with a rate the same year of 43, compared, for instance, with Nebraska and a rate of 17, had a death rate 2.5 times as great. Abroad the factor of urbanization may be partly measured by comparing the mortality of the capital cities against that of the entire countries. For instance, in 1935, the Paris rate, 169, exceeded that of France, 134, by 26 per cent; the rate of Rome, 127, was higher by 46 per cent than that of Italy, 87; in Spain, the rate of Madrid, 137, compared with that of 107 for the entire country was an excess of 28 per cent. On the other hand, in London the rise over the country as a whole, for the year 1936, was only 13 per cent—the rates being 78 and 69 respectively—but then there is perhaps less disparity between the industrial development of that center and of the remainder of England and Wales, with its many other cities, than is apt to be found on the continent.

**Color.**—With a colored population in the United States, according to the last census, of over 13 million, tuberculosis in this group presents a serious problem which is further complicated by the higher mortality rate which this race still suffers.

Nation-wide reports show the march of tuberculosis in the colored race is still far from being halted. In 1910, in the United States Registration Area, with a total of 86,309 tuberculosis deaths registered during that year the colored deaths—mostly those of Negroes, the remainder being Chinese, Japanese and Indian—numbered 9676 or 11 per cent of the total. At that time, however, a number of southern States were not in the Mortality Statistics Area. In 1940, in the entire Continental United States, of 60,428 tuberculosis deaths that year, 17,217 or 28 per cent were among the colored (for annual details see Table XV). There is some difficulty in interpreting the figures through that period since, first, as stated, they covered originally only a portion of the people of the entire country; secondly, the tuberculosis death rates during that time had declined at different rates in the two racial groups. A comparison can, however, be made for the Registration States between the years 1920 and 1940 (see Table XIV) where

TABLE XV  
PROPORTION OF COLORED TUBERCULOSIS DEATHS  
*United States Registration Area, 1910-1940*

Year	Tuberculosis Deaths		Per Cent Colored	Year	Tuberculosis Deaths		Per Cent Colored
	Total	Colored			Total	Colored	
1910	86,309	9,676	11%	1926	91,568	21,595	24%
1911	94,205	11,326	12%	1927	87,567	21,310	24%
1912	90,360	10,942	12%	1928	90,659	22,955	25%
1913	93,421	12,644	14%	1929	88,352	22,415	25%
1914	96,903	13,660	14%	1930	84,741	23,456	28%
1915	98,194	14,529	15%	1931	81,395	24,388	30%
1916	101,396	16,368	16%	1932	75,509	22,302	30%
1917	110,285	18,898	17%	1933	74,842	22,234	30%
1918	122,249	21,192	17%	1934	71,609	21,099	29%
1919	106,985	21,036	20%	1935	70,080	18,811	27%
1920	99,916	19,854	20%	1936	71,527	19,799	28%
1921	88,135	18,516	21%	1937	69,324	19,063	27%
1922	90,452	19,674	22%	1938	63,735	18,131	28%
1923	90,732	19,421	21%	1939	61,609	17,254	28%
1924	89,724	20,345	23%	1940	60,428	17,217	28%
1925	89,268	20,918	23%				

Note Based on figures Mortality Statistics, United States Bureau of the Census, for expanding Area covering, in 1910, 58 per cent of the country, and the entire Continental United States since 1933 During that period several southern states were added

it is found that among white males the tuberculosis death rate declined by 57 per cent and among the colored of the same sex by 45 per cent; among white females it fell by 71 per cent and in the colored by 56 per cent. During the last year of the period mentioned the death rates of the whites were 45 for the males and 28 for the females, among the colored, 139 for the males and 117 for the females.

The greater part of the Negro population still resides in certain southern States and tuberculosis death rates in the principal ones compared separately for the white and the colored between the years 1920 and 1940 show the situation and progress made (see Table IX). In Mississippi, for instance, the tuberculosis death rate in 1920 was 199 per 100,000 among the colored, and in 1940 it was 74; Florida, in 1920, 180, and in 1940, 112; in Georgia, in 1922, 141, and in 1940, 90;

in Louisiana in 1920, 234, and in 1940, 95. Comparatively high tuberculosis death rates still prevailed in certain States in 1940: Virginia, 124 per 100,000 population; Tennessee, 149; Kentucky, 162; Maryland, 238. A large number of Negroes migrated to cities, particularly in the industrial North, during the 1920's. The special survey by the writer for the year 1940 reveals that in 46 large communities, with a total population of 32 million in which were included more than three million colored (see Table VI), 33 per cent of the entire tuberculosis mortality occurred among the latter, their death rate that year being 196 per 100,000 population.

The ratio between the colored tuberculosis death rate and that of the whites, in the year 1940, was 3.1:1 for the males and 4.2:1 for the females. This proportion varies at certain ages; among those in their teens the disparity or excess of the colored death rate over the white is greatest: for males between the ages of 15 and 19 it was 10.0:1 (see Table XIV).

The higher tuberculosis rates among Negroes are found in spite of the fact that tuberculin testing, at least in childhood or for the same communities, reveals no significant difference in the frequency with which they are infected as compared with the whites. It would be ignoring facts to attempt to explain this difference in the mortality rates on the basis of greater opportunities for infection or on environmental conditions; they have their influence, yet they are not the main cause. Probably the most reliable, distinctive information and presentation of the subject has been made by Pinner and Casper<sup>44</sup> who studied evidence of the progress of tuberculosis in the American Negro by careful reviews of observations following autopsies upon whites and Negroes dying from this disease in Detroit and in Chicago. Comparing the frequency of "isolated phthisis" in Negroes and whites, they state: "If it be permitted to discuss features of resistance toward tuberculosis in patients dead of the disease, it surely must be conceded that the highest degree of resistance is present in those individuals in whom, in spite of extensive destruction of one organic system, the infection could not take hold by hematogenous or lymphatic propagation of distant organs. This type of lesion was present in nearly half of all white patients and in less than a third of Negroes . . . we have found calcified primary lesions in 25 per cent of whites and in 17.5 per cent of Negroes. . . . Information on duration of the disease was available, the total average for Negroes was 325 days and for the whites 995 days. . . . Cavities . . . without an organized wall and more or less filled with liquefied masses are much more frequent in Negroes." These authors add: "All attempts to explain the Negroes' lesser resistance to tuberculosis on the basis of lesser early tubercularization are without convincing proof and the conclusions deduced from them cannot be accepted." . . .

Pinner and Casper also say, "to produce a composite picture of what tuberculosis does in the Negro and in the whites, it would have to be said that one extreme is presented by the strictly localized fibrotic lesion, 'isolated phthisis,' and the other by massive exudative lesions and by hematogenous and lymphogenous spread. The former is the characteristic disease of the whites, the latter that of the Negro."

Roth<sup>45</sup> recently brought out the significant experience in the United States army among Negro and white troops during the period from 1922 to 1936.





pointing out that here with the careful physical examinations before enlistment and continuous attention by medical officers there was an opportunity to see under practically similar environment the influence of race on tuberculosis. Observations covered nearly 100,000 men annually. The average morbidity rate among white soldiers was 2.10 per 1000; the Negro rate only 2.56—not materially different, therefore, as regards the "breakdown rate" from tuberculosis. But, as Roth remarks: "For the 15-year period the total white death rate" was "0.24 per 1000 men, while the Negro rate" was "0.99, or a ratio very close to 4:1 to the disadvantage of the Negro. Thus it would seem, when this evidence is considered in conjunction with other surveys such as that of Green in Cleveland, and in view of the clinical and pathological differences which are to be recognized in the two races, that environment cannot be held to explain the differences in susceptibility to the disease which the two races so generally manifest." He concludes: "A slightly greater percentage of Negroes might be expected to contract the disease, but a considerably greater percentage of them would die from it."

But along with this evidence of a different rate of progress or development of tuberculous infection in the Negro, it should be noted that statistics available indicates among them, too, the possibility of material declines of their tuberculosis mortality from the very high level it was formerly. As previously noted, between 1920 and 1935 in the original Registration States alone there has been an average reduction of more than one-third in the colored tuberculosis mortality. In New York City, the death rate of Negroes in 1911 was 598 per 100,000; in 1943, 183, a sheer drop of 69 per cent in 33 years. For that matter, it might be said that at present the tuberculosis death rate of the Negroes in a large city like New York is less than that which important immigrant groups of whites had here only a few years ago. As recently as 1920, for instance, residents of New York born in Ireland suffered a death rate of 306 per 100,000. The writer sees in these higher tuberculosis death rates of the Negroes simply the conditions and rates that have prevailed among practically all races emigrating from agricultural sections or open-air life when they first go through the transition and shock of transplantation from the home and native soil to that of the industrialized, urbanized and congested communities (see also section on racial aspects of tuberculosis).

Considering sex among the colored, the death rates of the two are not materially different for the groups as a whole, 139 per 100,000 population among the males and 117 among the females (see Fig. 19). The rates vary, however, slightly at different periods of life, though somewhat in the same direction as among the whites. For instance, in the age group 20 to 25 the tuberculosis death rate of the colored female is higher than that of the male just as that of the white female of the same age; later in life, the tuberculosis mortality of the male exceeds that of the female among the colored just as among the whites. The colored group has the characteristic of higher mortality rates somewhat younger in life, just as formerly when the death rates of the whites were higher they were more apt to have the so-called "young adult type of phthisis" than now when their high rates occur at comparatively later periods of life. This shift of the tuberculosis peak

from comparative youth to older age has been a common observation in most racial groups studied as a wave of tuberculosis has spread through them.

**Occupation.**—With tuberculosis mortality comparatively under control among children in the United States—through extensive segregation in hospitals and sanatoria of active cases, consequently “breaking contact” so intimate at that age, and through cleanliness of food especially of milk now either from tuberculosis-free cattle or pasteurized—it is especially among adults that the disease now still causes extensive ravages, in fact being the chief cause of death among them at the most important and productive period of life. It stands to reason, therefore, that occupation and conditions of work are now reckoned to have the greatest influence here. But outside of studies among comparatively small groups of workers such as those exposed to silica dust, which have an undoubtedly high tuberculosis mortality, or among hospital workers which have received special attention lately, there were, until the study of this subject by Whitney\* in ten selected States, no really dependable up-to-date data that covered for this country representative sections of the large number of adults, men and women, that are employed nowadays outside of the home.

Reliance upon different rates, if they exist, of tuberculosis mortality between the two sexes at certain age periods of life to uncover, if possible, the influence of particular occupations is also of very limited value since it can be readily visualized that independent working conditions might yet have equal influences upon the death rate, that might then seem unaffected, though both might be at levels above the average.

Since the discussion as to the influence of occupation upon tuberculosis mortality must needs still be largely academic, perhaps it were wise, at least from a statistical standpoint, to put down certain essentials that should be met in the future to uncover or measure this factor. First of all, during adult life, especially in the United States, it should be realized that now the greater part of the day in cities is not spent at home, where, after all, one but visits and sleeps nowadays, but instead it is used up in travelling to and from places of employment in crowded trains, buses, and trolleys; secondly, at work in business offices, stores or industrial and manufacturing places; finally, in amusement and recreation outside of the home. Censuses in the future should include an additional and equally complete enumeration of the adult population at their place of work with proper qualifications as to the general nature or character of the enterprises and the particular type of position held there. Wisdom would also demand extra data, if possible, on hours of labor and wages; and, as in the ordinary census of home population, details of age, sex and nativity. Correspondingly and equally essential, there should be a new outlook upon the annotation and utilization of mortality records; at present these are generally and geographically distributed against the previous home addresses of the deceased. If the influence of daily occupation, outside of the home, is to be correlated with a day-working population census, likewise the mortality data must also be re-presented on a basis of the address where each deceased was formerly employed. Only when day-employ-

\*Whitney, J S : National Tuberculosis Association—Death Rates by Occupation, based upon data of the United States Census Bureau, 1930.

ment censuses are taken as well as home enumerations of the night population, and when mortality and sickness records are correlated against the work places and types of employment can a beginning be made at attacking with proper directness tuberculosis among adults where it mostly originates nowadays. Finally, it must be realized in the determination of tuberculosis rates among adults that, apart from the major influence of labor or work conditions, there are also qualifying conditions, such as the sanitary arrangements where one is employed, personal habits and economic status. The latter plays a great part both in increasing break-downs and upon the ability to secure treatment that may lead to recovery and the saving of life.

Only a few worthwhile or broad investigations are available for study as to the possible influence of occupation upon tuberculosis rates among adults. One relates to the study of the occupational mortality experience of the Metropolitan Life Insurance Company in 1922-1924, by Dublin and Vane<sup>16</sup>; a second, to the supplementary reports of the Registrar-General of England and Wales for the years 1921-1923 and for 1930-1932 on the mortality of men in certain occupations; a third, as already mentioned, is the study by Whitney of death rates among occupied males in ten important States during the year 1930; a fourth, made available recently by the Dominion Bureau of Statistics,<sup>17</sup> is the special report on occupational mortality in Canada during 1931 and 1932.

The Metropolitan report was of necessity a study of the proportion of tuberculosis deaths in a given group, not necessarily of the rate of that group in the general community to the total employed in the same industry; but its conclusions follow very much lines of common knowledge as to the hazards to health in certain industries. In general, the greatest amount of tuberculosis in the Metropolitan Life experience was found among those exposed to dusts that undoubtedly damage the lungs, these are "miners underground," excluding coal miners; pottery workers; stone cutters; cutlers and grinders. Then followed waiters, hotel servants; cigarette, and tobacco workers; laundry workers; compositors, printers and pressmen; also, with high rates, were brass foundry workers, glass workers; clerks; polishers; barbers, hairdressers; tailors; furniture workers, and so forth. The groups with lower relative indices for tuberculosis of the respiratory system were watchmen, merchants, blacksmiths, streetcleaners, policemen, firemen, coal miners, and so forth—among whom obviously there are indications of a selective influence in that these trades are apt to require more able-bodied workers.

The 1921-1923 report for England and Wales indicated high tuberculosis rates among certain workers in the order named: tin and copper miners, cutlers and grinders, hawkers, file workers, lead miners, hotel servants, waiters, broom workers, barbers, seamen, messengers, porters, gunsmiths, brass workers, shoe workers, stevedores, dock laborers, book binders, printers, tool workers, hairdressers, chimney sweeps, musicians, workers in lead manufactures, leather goods, glass manufacture, law clerks, wood turners, pottery workers, textile cutters, cabinet workers, stone quarriers, commercial clerks, coal heavers, slaters, stone cutters and masons, warehouse men, tobacco operatives.

Among those with low tuberculosis rates, in the employed groups aged 25 to 65 in England and Wales, were then noted the following: clergymen, game-

keepers, farmers, barristers, railroad engineers, surveyors, physicians, school masters, agricultural laborers, brick makers, coal miners, druggists, shipbuilders, civil service employees, grocers, railway officials, bank and insurance officials, building foremen.

A similar investigation of occupational mortality in England and Wales during the three-year period, 1930-1932, showed among occupied males 20 to 65 years of age a higher mortality ratio than the average for the entire group of workers—taken as 100—particularly among the following: metal grinders (275), potters (233), glazers (230), barmen (212), costermongers (200), boot and shoe workers (188), water transport and dock laborers (186), masons and stone cutters (179), waiters (178), hairdressers (162), porters (160), inn-keepers (148), general laborers (146), all of whom therefore with tuberculosis death rates in excess of that of employed men anywhere from 46 to 175 per cent.

Among male workers with a tuberculosis ratio in 1930-1932 lower than that of the standard (100) were particularly "proprietors" (60), professional engineers (58), agricultural laborers (51), teachers (51), policemen (51), wool textile weavers (50), employers and managers (48), railway engine drivers (47), bank (46) and railway officials (43), physicians (44), farmers (35), civil service officials (35) and clergymen (25).

Among occupied single women in 1930-1932, in England and Wales, those with a higher tuberculosis mortality ratio than the average of the entire group of working women included french polishers (200), textile workers especially spinners (183), milliners (163), laundry workers (151), workers in chemical processes (150), with mortality ratios therefore anywhere from 50 to 100 per cent in excess.

Employed women with a tuberculosis ratio half or less than that of the standard were those assisting on farms (50), teachers (48) and telephone operators (47). The large group of typists and clerks had a mortality ratio of 75 or 25 per cent lower than the average.

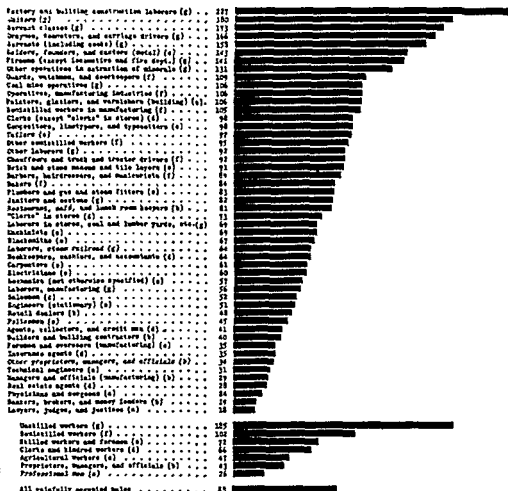
It is obvious in general that in the trades where workers are exposed to hard dusts or possibly where low wages prevail that the tuberculosis death rates are unduly high; secondly, that in those occupations where the employee works more or less in the open air or where there is required a greater physical ability, or where remuneration is higher, that there are found lower tuberculosis rates.

The study by Whitney, based upon reports of the United States Bureau of the Census for the year 1930, covered occupied males between the ages of 15 and 65 in ten selected states. It was found (see Fig. 26) that, on an average, a death rate from pulmonary tuberculosis of 88 per 100,000 prevailed. Professional men suffered a mortality of only 26; proprietors, managers and officials, 43; agricultural workers, 47; clerks and "kindred workers," 66; skilled workers and foremen, 72; semiskilled workers, 102; and unskilled workers, 185. The differences in tuberculosis mortality of these occupied men were obviously due in great part to economic conditions surrounding their labor as well as its nature; also, noticing the high rates among waiters and servant classes, 180 and 173 respectively, one may question whether account has been taken therein of color or race which, regardless of occupation, plays its own and often important part in tuberculosis.

# PULMONARY TUBERCULOSIS DEATH RATE ACCORDING TO OCCUPATION

## PULMONARY TUBERCULOSIS

DEATH RATE—PER 100,000 OCCUPIED MALES (15-64 YEARS OF AGE) IN TEN STATES\*  
DURING THE YEAR 1932



\*States listed in parentheses refer to occupations included in the seven general groups. \*Standardized according to age distribution of all gainfully occupied males in the selected states. Alabama, Connecticut, Illinois, Kansas, Massachusetts, Minnesota, New Jersey, New York, Ohio, and Wisconsin. From "Death Rates by Occupation" by J. S. Whitney, National Tuberculosis Association. (Chart by Research Service, NEW YORK TUBERCULOSIS AND HEALTH ASSOCIATION)

Fig. 26.

The Canadian report is based on an analysis of 38,746 deaths from all causes which occurred during the two years 1931 and 1932 among "all males aged 20 to 65 years which totalled at the time of the 1931 census 2,889,149." Among these men, 4516 deaths from tuberculosis of the respiratory system were recorded, an average annual rate of 78 per 100,000 workers (see Fig. 27). Owners and managers, in manufacturing, experienced a mortality rate of only 22; a similar group, in transportation concerns, 28; teachers, lecturers, professors, 46; owners and managers, all trades, 52; farmers, 59. But office workers suffered a mortality above the average, 88; workers in coal mining had a death rate of 96; laborers,

other than agricultural, 124; fishermen, 168; operatives in manufacturing non-metallic mineral products, a rate of 205 or nearly nine times the rate of the lowest group. Here, too, in Canada, the differences must in greater part be due to the character of the labor and economic conditions of the personnel or workers. Care should, however, be taken when interpreting these reports in that country to remember that in certain of the occupations there may be a greater preponderance of workers of French ancestry who, in general, suffer at present more from tuberculosis than do those of Anglo-Saxon origin.

Crouch<sup>48</sup> has called attention recently to the extremely high tuberculosis rates among miners in Silver Bow County, Montana. For the period 1919 to 1933 he found an annual death rate of 755 per 100,000 among these workers whereas in the remaining adult male population it was 180; among adult females, 43; and, in children under 20 years, 19.

Recently, several careful observers have called attention to the greater dangers from tuberculosis to which the nursing and medical professions, especially during their training periods, are exposed. Heimbeck, first of all, in Oslo, Norway, drew attention to the situation among pupil nurses in the hospital of Ullevaal where an unusual proportion among those found free from tuberculous infection on entering had developed cases of tuberculosis afterward. Significant, however, was the accompanying information that no such undue proportion of tuberculosis followed among those who on entrance reacted to the tuberculin test and were therefore previously infected. In Manitoba, Ross<sup>49</sup> likewise has drawn attention to the unusual proportion of nurses requiring treatment for tuberculosis at the provincial sanatorium. In Minnesota, both Myers<sup>50</sup> and Geer<sup>51</sup> have also called attention to the unusual prevalence of tuberculosis among student nurses. Geer reports that at the Ancker Hospital in St. Paul, first, and rather interestingly, that of the nurses entering training 30 per cent reacted to tuberculin test—in other words, 70 per cent were uninfected and this is perhaps most suggestive of a particular condition in that group of workers who in American hospitals are to an unusual degree recruited from the country rather than from city sections—; secondly, of 112 young women entering during a recent two-year period, six or 5 per cent developed tuberculous disease, but five of these it must be noted had not reacted to tuberculin when first tested on admission.

Undoubtedly the opportunities for infection in hospital work are greater than in other places of the community. Secondly, there is a danger that, between arduous ward duty, studies and time spent in amusement, an undue strain is placed upon these young women. It must be noted again that cases of tuberculous disease are appearing mostly among those previously uninfected, and it raises the fundamental question whether such types elsewhere, practically virgin soil, would not display an equally unusual amount of tuberculosis when exposed to city life, under congested and similarly difficult work conditions. But in such individuals long and arduous employment in contact with open cases of tuberculosis is most dangerous.

Under perhaps similar conditions are also medical students. At Yale University, Soper and Wilson<sup>14</sup> report in the entering class of medical students a higher proportion with a positive tuberculin test than, for instance, in slightly

older students in the other schools. The studies of Hetherington, McPhedran, Landis and Opie<sup>13</sup> among students at the University of Pennsylvania shed further light upon this group. First, should be noted the experience at that place that first-year medical men and first-year college men both were found equally infected, namely, 84.8 per cent reacting as against 84.4. But upon repeated tests through their four years, it was found that the college men of the senior year still had 84 per cent reactors and the fourth year medical men 98 per cent.

**CANADA — TUBERCULOSIS OF THE RESPIRATORY SYSTEM**  
DEATH RATES\* OF OCCUPIED MALES, AGES 20-64 YEARS,  
DURING THE TWO-YEAR PERIOD, 1931-1932†

OCCUPATIONS (selected)

Workers Totals Annual RATES per 100,000 workers  
Exposed Deaths

Operatives, mfg non-metallic mineral products . . .	5,565	23	205
Workers, mining (non coal), milling, pulp, oil, gas wells . . .	26,994	21	172
Fishermen . . .	21,842	43	153
Operatives, leather tanning and manufacture . . .	34,451	52	151
Laborers (other than agricultural) . . .	391,339	976	124
Barbers, hairdressers and manicurists . . .	15,496	39	120
Other workers, personal service, including cooks . . .	39,456	179	120
Painters, decorators and glaziers . . .	32,817	65	104
Lumbermen . . .	35,961	69	99
Brick and stone masons . . .	10,036	23	99
Workers in coal mining . . .	74,183	61	96
Plumbers, gas and steam fitters . . .	15,171	30	94
Office workers (including public officials) . . .	131,400	213	83
Hotel, restaurant, lodging, concert, managers . . .	13,742	23	81
Textile goods, wearing apparel workers . . .	26,575	43	82
Salesmen (other than commercial travellers) . . .	84,470	136	81
Professional engineers . . .	15,439	25	81
Hotel operatives, not machinists, motor mechanics . . .	64,816	70	79
Carpenters . . .	73,409	114	75
Clergymen . . .	11,533	14	76
Compositors and printers . . .	11,741	14	75
Cooks, bakers, other industries than specified . . .	30,390	29	75
Blacksmiths, harnessmen and farriers . . .	14,177	23	74
Electricians and wiremen . . .	20,168	32	74
Professional workers (other than specified) . . .	31,560	49	74
Motor, air mechanics, other mechanics not specified . . .	40,435	60	73
Chauffeurs, drivers, golfers . . .	79,174	207	64
Meat, confectionery, biscuit makers . . .	10,195	13	64
Physicians and surgeons . . .	8,793	13	64
Farriers . . .	10,427	23	64
Commercial travellers, sales agents . . .	21,905	27	59
Farmers . . .	618,727	117	59
Machinists and toolmakers . . .	32,063	34	55
Owners and managers, all trade . . .	99,675	104	52
Lawyers, notaries, justices, magistrates . . .	7,649	9	51
Stationary engineers and firemen . . .	26,336	26	53
Operatives, manufacture wood products . . .	27,247	22	50
Other operatives, printing, publishing, book binding . . .	5,345	5	45
Teachers, instructors, professors, principals . . .	20,042	20	44
Conductors, brakemen, baggage men, street railways . . .	14,852	14	39
Locomotive engineers and firemen . . .	13,109	11	34
Owners and managers, transportation . . .	11,568	10	25
Owners and managers, manufacturing . . .	30,050	15	22
Total specified . . .	2,371,730	3,720	..

ALL MALES AGES 20-64 YEARS . . . . . 2,609,149 4,516 75

\*Rates—Standardized according to age distribution of all males, 20-64 years, Canadian Census, 1931. — From Report, Occupational Mortality in Canada, 1931-32, DOMINION BUREAU OF STATISTICS. — †Pulmonary tuberculosis deaths during two-year period, 1931-32. — (Chart, G. J. Drolet, NEW YORK TUBERCULOSIS AND HEALTH ASSOCIATION).

Fig. 27.

Further, among 279 college men only one case of manifest pulmonary disease developed, while among 452 medical men 14 such occurred, of which 13 were among the third and fourth year students. It should be added, however, that the average age of the college men ran between 18 and 21 years and that of the medical men between 22 and 24.

Among both student nurses and medical students we are, therefore, witnessing instances of tuberculosis due to closer or more intimate contact with open sources of infection—apart from breakdowns that might be due to excessive study and trying work conditions in these occupations themselves.

One extreme difficulty in interpreting tuberculosis rates in any group is to appraise the value of a particular, single factor where it must be acknowledged that the net results are constantly affected by certain basic conditions: first, those of "seed," namely, in infection the dosage and the frequency, often varying; second, of the "soil," the constitution of the individual, namely, the racial stock from which he sprung and the relative immunity or susceptibility to tuberculosis it possessed; also, the age or growth attained; lastly, the environment or the living and working conditions. All these have a definite influence, and the final resultant picture seen has been colored in a variety of ways by combinations of these factors that are at work all the time.

**Housing.**—With tuberculosis mortality generally greatest at present in the large cities, it also stands to reason that housing conditions should be considered to have weight in affecting mortality. However, there is the difficulty, in appraising this factor singly, that it is only part of a picture largely ruled by the economic condition of the family, which itself may greatly influence other things like quantity and quality of food available, work and rest hours, as well as opportunity or lack of ability to get early and adequate medical or institutional care so important in such a disease. But the similarity of findings as to a greater prevalence or a higher mortality rate in parts of large cities where housing conditions are obviously inferior demand recognition in tuberculosis. Distribution maps of pulmonary tuberculosis records in New York City made by the writer<sup>52</sup> for the period 1915-1920 in both Manhattan and Brooklyn reveal in each instance, as for that matter was similarly observed by Billings<sup>53</sup> 30 years previously, that generally speaking the areas with highest mortality were usually found to be where the housing was poorest. In the Manhattan study, for instance, whereas the pulmonary tuberculosis death rate was only 25 per 100,000 in areas with individual rich homes as on Fifth Avenue and bordering Central Park, on the other hand on the Lower West Side, where housing conditions of 50 years ago still prevail, the death rates in some instances were ten times as high. Similarly, in Brooklyn, the death rates in the older sections in Fort Greene or Red Hook were several times those in the more well-to-do and better housed sections of the borough.

In New York City, there is difficulty in appraising the weight of housing between different sections if the predominating racial groups are not the same, but an interesting measure of perhaps just and only the housing factor was found by the writer in a study made in 1922 of the pulmonary tuberculosis death rate in three different Jewish sections. In the older Gouverneur district downtown, the pulmonary tuberculosis death rate that year was 83 per 100,000; in the Mt. Sinai district in upper Manhattan, where housing was comparatively better and of more recent construction, the death rate the same year was 65; again, for that same group, mainly Jewish, it was found in Tremont, in the Bronx, where new housing had been erected but a few years previously, following new subway transportation extensions, at that time the pulmonary tuberculosis death rate was only 52; finally in certain residential sections of Brooklyn where Jewish people lived in individual homes it was as low as 35—in other words as housing improved, likewise did tuberculosis come down. In Paris, studies, also made by



the writer during the World War, of the death rate from tuberculosis in various "quartiers" brought out the same difference: the death rate in the 20th "Arrondissement," a comparatively poor section, was several times that, for instance, of the 8th which has such well-known comfortable sections as the Champs Elysées. More recently the writer<sup>54</sup> has also studied the incidence of pulmonary tuberculosis, both from the morbidity and mortality records, of each of the five boroughs of New York City and in every instance the highest rates were found in the older sections: in Manhattan, in the Lower West Side district; in Brooklyn, in the Red Hook, Fort Greene, Bedford and Williamsburg sections; in the Bronx, in the Mott Haven part; and, in Queens, in the Long Island City section.

In the Bellevue-Yorkville district of New York City<sup>55</sup> during the five-year period, 1927-1931, in a sanitary area where the average rental paid for apartments was the highest in the district, namely, \$200 monthly, the tuberculosis death rate was only 19 per 100,000 population; but, in another where room rents averaged \$35 only the tuberculosis death rate was 256. Similarly, in Cleveland, Green<sup>56</sup> studying the correlation of housing and tuberculosis, more specifically according to the 1930 Census reports of the rent paid in certain areas compared with the tuberculosis mortality during the four-year period, 1928-1931, in the same sections, found the white tuberculosis death rate where the highest rents were paid was only 19—as in New York—whereas it was 127 where the lowest rents only could be paid. The same ratio was noted among the colored in Cleveland, namely, that the tuberculosis death rate increased in this racial group as we pass from those able to pay a certain high rent and secure proper quarters to those who could afford only a low one.

Haven Emerson has well remarked that, in New York City, it is in sections where houses 50 years old are still in use that one finds tuberculosis death rates common to the community 50 years ago.

It is not amiss to note here that it is felt in New York City that one of the measures, of a generation ago, which most favorably affected the tuberculosis situation was the passage of the so-called tenement house law that prevented the further erection of dwellings with unventilated or dark rooms so common previously.

**Race.**—The extent to which racial origin influences tuberculosis mortality nowadays, especially in the United States where there are foreign-born groups of such unusual size, is perhaps—outside of the colored who have already been considered as compared with the whites—not as great for those from certain parts of Europe as was common a few years ago. This has largely taken place because, first, immigration has been more and more limited and, secondly, because of the extensive public health measures and the increase of institutional beds for the care of the sick which gradually are bringing the disease under control.

Groups with a colored strain, such as from Puerto Rico, Cuba or the Philippines, and the Mexicans with their large admixture of Indian blood still suffer very high mortality rates when exposed to the dangers and congestion of American city life. Among other foreign stock, especially from Europe, what is striking to notice is that while their tuberculosis death rate does not seem excessive

TABLE XVI

TUBERCULOSIS MORTALITY† ACCORDING TO NATIVITY, COLOR, AND RACIAL GROUP—  
New York City, During Two-Year Period, 1930-1931

## A.—AMONG THE NATIVE AND FOREIGN-BORN

Nativity	Federal Census 1930 New York	Pul- monary		Non- Pulmonary		All Forms Tuberculosis			
		2-Yr. Period		2-Yr. Period		Deaths Year		2-Yr. Period	
		Annually		Annually				Annually	
		Deaths		Deaths				Deaths	
		No.	Rate‡	No.	Rate‡	1930	1931	No.	Rate‡
Native-born:									
Puerto Rico	44,908	176	391	19	43	207	183	195	434
United States.	*4,526,852	2,585	57	415	9	3,062	2,938	3,000	66
Total° . .	4,571,760	2,761	60	434	10	3,269	3,121	3,195	70
Foreign-born: Total°	2,358,686	1,653	70	158	7	1,820	1,801	1,811	77
New York City .	6,930,446	4,414	63.7	592	8.5	5,089	4,922	5,006	72

## B.—AMONG THE WHITE AND COLORED RACES

White (Native, foreign-born) . .	**6,589,377	3,519	53	442	7	4,072	3,849	3,961	60
Colored.									
Negro									
Puerto Rico .	9,951	59	588	7	75	68	64	66	663
United States	263,001	684	260	120	46	780	827	804	306
Other countries°°	54,754	97	178	18	33	123	108	115	211
All Negro . . .	327,706	840	257	145	44	971	999	985	301
Other colored‡	13,363	55	412	5	37	46	74	60	449
All colored . . .	341,069	895	262	150	44	1,017	1,073	1,045	306
Total, all races . .	6,930,446	4,414	63.7	592	8.5	5,089	4,922	5,006	72

† Classified according to nativity or birthplace of deceased. ‡ Per 100,000 population. ° White and colored. °° Cuba, other West Indies, etc. † Includes Chinese, Japanese, Indian and a few other colored. \* Including 8,219 born in "outlying possessions other than Puerto Rico" whose deaths were not classified separately. \*\* Including 2,152 Mexicans entered as whites.

Based upon special tabulation by Department of Health, City of New York (Weekly Bull. Oct. 8, 1932) with rearrangements—especially by nativity and among the colored by birthplace.

compared with that which they suffered only a decade ago, their ratios still range themselves in a somewhat similar order.

In reviewing this situation of tuberculosis among different racial groups it is wise to recall, as noted in previous sections, that in tuberculin test surveys where at the same time the racial origin or extraction of the children has been noted no significant difference in the numbers found infected has been recorded. Outside, perhaps, of exceptional cases in infancy, within the same communities the opportunities for infection are fairly similar and common. In Philadelphia, the school children tested by the staff of the Phipps Institute showed 75 per cent of the Jewish children reacting compared, for instance, with 73 per cent of the colored; and, yet, everyone is aware of the different mortality rates of the two

TABLE XVI (Continued)  
(—BY COUNTRY OF BIRTH)

Nativity	Federal Census 1930 New York	Pul- monary		Non- Pulmonary		All Forms Tuberculosis			
		2-Yr. Period		2-Yr. Period		Deaths Year		2-Yr. Period	
		Annually		Annually				Annually	
		Deaths		Deaths				Deaths	
		No.	Rate‡	No.	Rate‡	1930	1931	No.	Rate‡
China	6,629	39	581	3	45	29	54	42	626
Puerto Rico. White	34,756	117	335	12	35	139	118	129	370
Colored (All)‡	10,152	59	581	7	74	68	65	66	655
Total	44,908	176	391	19	43	207	183	195	434
Japan	1,871	7	374	0 5	27	6	9	7 5	401
Ireland	220,631	280	127	24	11	306	301	304	138
Cuba, other W. Ind									
White	13,032	7	50	0	0	6	7	7	50
Colored (All)‡	48,263	55	114	9	19	61	67	64	133
Total	61,295	62	100	9	15	67	74	71	115
Scandinavia	86,493	72	84	5	6	77	78	77	90
Austria-Hungary	187,052	146	78	10	5	156	156	156	83
United States. White	4,259,069	1,892	44	294	7	2,271	2,101	2,186	51
Colored (All)‡	267,783	693	259	121	45	791	837	814	304
Total	*4,526,852	2,585	57	415	9	3,062	2,938	3,000	66
England	78,003	47	61	1 5	2	54	44	49	63
Italy	440,250	233	53	28	6	260	262	261	59
Russia	442,431	222	50	13	3	243	227	235	53
Germany	237,588	107	45	15	6	121	123	122	51
Poland	238,339	100	42	9	4	104	113	109	46
Other countries	**358,104	338	95	40	11	397	360	378	106
New York City	6,930,446	4,414	63 7	592	8 5	5,089	4,922	5,006	72

† Classified according to nativity or birthplace of deceased. ‡ Per 100,000 population. \* White and colored. \*\* Cuba, other West Indies, etc. † Includes Chinese, Japanese, Indian and a few other colored. \* Including 8,219 born in "outlying possessions other than Puerto Rico" whose deaths were not classified separately. \*\* Including 2,152 Mexicans entered as whites.

Based upon special tabulation by Department of Health, City of New York (Weekly Bull. Oct. 8, 1932) with rearrangements—especially by nativity and among the colored by birthplace.

groups. Similarly, in New York City, Asserson,<sup>5</sup> among babies tested, found those of different racial origin infected at practically the same rates and yet in her follow-up of positive reactors, eight per cent of the Irish babies died compared with five per cent of the Italian, 3.5 per cent of the American and 1.2 per cent of the Jewish. In Honolulu, Doolittle<sup>17</sup> remarks, of the Japanese junior high school students 74 per cent reacted, and among those part-Hawaiian, 73 per cent were positive, but the average mortality rate of the second group was 13 per cent in excess of that of the Japanese. Dublin and Baker<sup>57</sup> several years ago, in their study of the mortality of foreign race stocks in Pennsylvania and New York State, found the familiar alignment of high mortality rates among the Irish-born and of comparatively low rates among Italians and especially among groups from Russia and Austria-Hungary, mostly Jewish.

The writer,<sup>58</sup> studying in New York City, during the four-year period, 1918-1921, the mortality according to the then leading racial groups, found extremely high rates among those from Finland, Ireland, Norway, Switzerland and Sweden; and, on the other hand, lower rates among native-born in the United States and those from Rumania and Russia, the latter two including many of Jewish origin.

Similarly, the writer has again studied during the two-year period, 1930-1931, the tuberculosis mortality in New York City according to racial origin (see Table XVI). First, should be noted that, whereas the city then had an annual average tuberculosis death rate of 72 per 100,000, the mortality of the native-born in the United States was 66 and that of the foreign-born 77, an excess, for the latter, of some 16 per cent. On the basis of color, it was found that the whites had a tuberculosis death rate of 60, and the colored of 306, five times as great. The second group, however, includes here several important but different sections, namely, besides Negroes, the Chinese and Japanese. Thus, while the tuberculosis death rate of Negroes born in the United States and now living in New York City was 306, that of Negroes born in Puerto Rico was 663, nearly ten times the death rate of the whites in the city here. The Chinese likewise, although it must be recalled they have an unusual proportion of male adults, suffered a tuberculosis death rate of 626, while among the Japanese the rate was 401.

Among the foreign-born white, it was found that, while the city rate averaged 72 for 100,000 during the two-year period, 1930-1931, that again among those born in Ireland it was nearly twice as high, namely, 138; Scandinavians had a tuberculosis death rate of 90; those born in England, 63; in Italy, 69. The lowest rate, 46, was among those born in Poland which include many Jews.

Many opinions have been given to explain these differences: The colored, to defend themselves against the stigma of inferior resistance, will complain of their suffering adversely from undue economic pressure; charges of bad personal habits, as to food or drink, have been hurled against other victims. Certain writers have denied or refused to look at the evidence of these different mortality rates, repeating themselves in place after place or time and again, and still before our eyes. But this much in general must be observed: the high mortality rates are found especially among groups formerly following agricultural pursuits in sparsely settled spaces or given to living in the open air; and, on the other hand, it is especially those who have been town dwellers for some time or in greater proportion than others that now have the lowest mortality rates. Mere chance or different opportunities for infection cannot explain why the same groups should always be numbered among the favored or unfortunates.

Fishberg,<sup>59</sup> most correctly, it seems, describes what has happened: There was a time, "in Vienna" when among Jews, "during 1648 to 1649, of 863 registered deaths, 278 were attributed to 'consumptive causes.'" His further remarks on race influence are also very illuminating. As he says: "Bearing in mind the facts . . . it appears that tuberculosis is inherently not a racial problem; there are no races which are more vulnerable to the disease because of phylogenetic

peculiarities . . . which distinguish one race from another. One human race or group, when first encountering the tubercle bacillus, is as vulnerable as another. It is only after they have been exposed to infection for many generations that they acquire a certain degree of resistance which, when it does occur, is liable to cause milder clinical forms of the disease than when occurring in races that are virgin soil to the bacilli."

Bogen<sup>60</sup> also furnishes similar evidence, on the other side of the North American continent, of the usual differences in the United States in the mortality from tuberculosis of various racial stocks: In the follow-up of patients treated at the Olive View Sanatorium in California he found, among others, that 58 per cent of the Negro cases died, 49 per cent of those of "Norse" origin, 40 per cent of the Irish, 34 per cent of the American and 26 per cent of the Jewish.

Another example of how this process has been repeating itself on the opposite side of the globe, following similar conditions, is found in the tuberculosis death rates of Calcutta among the two large groups of Mohammedans and Hindus, according to the report of the local health officer, Majundar.<sup>61</sup> The first had, for instance, in 1927, a rate of 360 per 100,000 population, whereas among the second it was 270. In other words, among the descendants of men from Mosul (Musulmans)—a nonindigenous group—a higher tuberculosis mortality occurs since they have migrated to or settled into a new congested center of population as compared with the rate of the native inhabitants.

### INHERITANCE.

It was not among nurses with "tuberculous diathesis" that Heimbeck, at the Ullevaal Hospital of Oslo, Norway, or Geer,<sup>54</sup> at the Apcker Hospital in St. Paul, observed the more frequent appearance and development of tuberculosis cases but rather among those, comparatively virgin soil, who had not reacted to tuberculin on admission for training.

Even early in life, the course of tuberculous infection, when it takes place in certain racial groups or families, is modified differently according to whether we are dealing with stock known to have been comparatively more frequently infected in the past than another which has had a shorter period of tuberculization.

If we accept, as we must, that the course of secondary infections is modified in individuals where there has been a previous infection, why should we refuse to see the possibilities of such similar modification in the course of two generations where the parent was already tuberculized and the child later exposed to a so-called primary infection—but practically secondary in that flesh. Is there not, after all, some continuance of the spark and thread of life between parent and child, that we should refuse cognizance of influence from such an origin and that from practically virgin soil?\*

\* Specific evidence of this possibility is unconsciously furnished by Cummins<sup>62</sup> in his 1926 Biggs Memorial Tuberculosis Lecture. Discussing natural and modified types of tuberculosis, he referred to two children as follows: "This little patient (picture that of a well nourished child) represents an approximation to the natural type of tuberculosis in a child. Her disease was pyrexial and she only survived about a year . . ." The other child "(picture, that of an emaciated girl) illustrating," he says, "the fact that the modified type of tuberculosis may occur even in childhood. This little girl was the child of an infected mother . . . her illness was extremely chronic and she lasted for over two years in the hospital . . ."

That, at present under city life where opportunities for infection are practically ubiquitous and common to all racial stocks, members of the colored race, for instance, should almost invariably suffer high mortality rates from tuberculosis and, on the other hand, those of Jewish extraction should have a mortality from that disease several times less, and that this order should repeat itself in many places always in the same direction—or again similarly as between Norwegian stock compared with Italian, or between Irish and English—compel the conclusion that there is at work through it all a hereditary factor. Whether such a factor in tuberculosis be one unfavorable, as Pearson,<sup>63</sup> for instance, would have it and that there be inherited a supposed tuberculous diathesis; or, as others who, like the writer, would have it a favorable one, namely, that what is inherited through tuberculous parentage is a comparative familiarity or ability to control infection somewhat better, need not be stressed immediately, but let us restate certain observations.

Several years ago, the writer,<sup>64</sup> from his own studies at Bellevue Hospital, New York City, observed, first, that in the children studied there were fewer clinical or manifest cases of tuberculosis appearing where there was a parental history of tuberculosis than where such was not known, and, secondly, that where the disease did establish itself, recovery took place more frequently in the positive history group than in the negative group. Against the first finding, several objections have been made; one, that among the survivors were not included a number of children who might have died previously from tuberculosis in a greater proportion in the positive parentage group than in the other; probably that point was well taken. Then it was further argued that in the division of the histories into groups with and without a history of tuberculosis in the parents there might have been deficiencies due to the difficulty of ascertaining such; but to this should be answered that the division of the records was based not upon mere history taking as is sometimes done in statistical offices but from only records of persons "medically examined" by tuberculosis specialists as is common in the tuberculosis dispensaries of New York, where it is customary to go over all family members concerned whether adults or children. Again, it was argued that the control group of children or adults without tuberculosis was drawn from a clientele attending the tuberculosis dispensary and therefore not a representative sample of the general population. This also ignored that, in New York City, such tuberculosis dispensary services are practically the only available general health examination facilities for many welfare and relief societies, which make it a practice to have all the members of the families under their care examined, so that in reality these institutions are largely chest clinics where specialists in tuberculosis examine a pretty general type of population. As a matter of fact, the proportion of non-tuberculous persons seen there far exceeds, from five to one or ten to one, the tuberculous patients.

The second observation of a greater rate of recovery among cases where one or the other parent had had tuberculosis has since been confirmed by others. For instance, Ford,<sup>65</sup> Tuberculosis Officer in Hertfordshire, England, has noted that among cases of pulmonary tuberculosis where the maternal history was

positive the prognosis, checked by follow-up work, was more favorable; in a total of 1062 patients, where the mother had had tuberculosis there was a lesser proportion of acute cases, 7.5 per cent, whereas where there was no parental history of tuberculosis the proportion of acute cases was higher, 10.3 per cent. Secondly, among 599 cases whose condition was known ten years after onset of the disease, there were only 12.0 per cent alive where there was no family history of tuberculosis; whereas, among the cases with a "direct maternal history," 20.6 per cent were alive. Ford concludes "those cases, where mothers suffered from tuberculosis, appear to do much better than the others."

On the European continent, Stephani-Cherbuliez,<sup>66</sup> referring to "influence of familial tuberculosis on the frequency of the disease" says, "of 3000 cases examined in the sanatorium of Hauteville, 59 per cent came from families free from tuberculosis and 41 per cent from tuberculous families"; secondly, as to the same influence upon the form or course of the disease that, "the fact of a pulmonary case being issued from a tuberculous parent increases by 20 per cent the chances which he will have of the evolution being benign." The same observer also studied the histories of 1017 cases of pulmonary tuberculosis at the Sanatorium, Victor Emanuel, III; again, it was noticed that the majority of patients were drawn from families whose parents were "sound"; secondly, that of 100 cases from "sound" families 26 only vanquished the disease whereas 36 did so among the children of the tuberculous. The author concludes: "*Chez les descendants de parents exempts de tuberculose, les formes chroniques graves, ou fatales, prédominent. Chez les descendants de parents tuberculeux ce sont au contraire les formes bénignes qui sont de beaucoup les plus nombreuses.*" Similar observations have been voiced in an extensive review by Sanarelli,<sup>67</sup> director of the Hygienic Institute of the University of Rome.

Let us refer again to the observations of Asserson among infants in New York City infected with tuberculosis that were followed up for five years. Certainly it would be a stretch of imagination to expect that within a couple of years there would be sufficient time for different opportunities through repeated infections to influence unequally the death rate according to racial stock. And yet, starting from the basic fact that the infants observed whether American born, colored, or of Irish, Jewish or Italian extraction were infected in practically equal frequency, the mortality rates were strikingly different and again according to whether one dealt with a group long known to be tuberculized or another not so long in contact with tuberculosis. The mortality of the Jewish babies was only 1.2, whereas that of the colored was 6 per cent, that of the Italian children 5.

There would seem to be no doubt that the acquirement and transmission of some degree of resistance by those exposed to tuberculosis is the only general explanation that would fit into those everyday racial differences which practically all coincide with the fact that high rates are found among groups that have been exposed to tuberculosis for a comparatively shorter time and low rates in the groups that have been more or longer exposed.

Remarks of Cummins<sup>68</sup> on this subject are interesting: "Is there any such thing," says he, "as 'acquired immunity' in tuberculosis? It has become fashion-

able in recent years to deny its existence but many, including the writer, believe it to be a factor of fundamental importance underlying and very largely explaining the difference between individuals, families and races in their power of resistance to the disease." Similarly, when discussing *inherited resistance*, Miller and Rappaport<sup>3</sup> remark: "In our effort to understand the remarkable changes which have occurred in the epidemiologic evolution of tuberculosis we are unable to escape the conclusion that succeeding generations which have been exposed to tuberculosis do not react in the same way as those not so exposed. This would appear to imply that some inherited change in the reaction of the individuals of later generations has occurred because of the experience of the preceding ones, and that consequently something in the nature of increased capacity to acquire resistance has been passed on through inheritance. We do not pretend to know just how this occurs . . . But in any event we believe that there is a very definite factor of inherited resistance which may explain many of the problems in tuberculosis as it is seen in individuals and as it is exemplified in families or in races. . . . The resistance of the race depends on the level in the immunity scale on which the majority of the individuals rest, and races will rise in this scale according to past tubercularization."

One might therefore generalize by saying that—at least as far as constitutional behavior is possible independent of environmental conditions—resistance to tuberculosis is in proportion to the health and especially to the extent of the previous tubercularization of an individual and his forbears.

The great difficulty, of course, in disentangling and estimating the influence of just and only the factor of inheritance has been the fact that it must be studied where the opportunities for infection by mere contact are greater even than where there is no tuberculosis in the parents. And yet the success of the Bang method in Denmark of separating new-born calves from infected herds or that of the Oeuvre Grancher in France by placing children of tuberculous families in the country should be sufficient evidence of what really takes place: Healthy offspring from tuberculous stock where post-natal infection is prevented.

A final and greatest difficulty in recognizing the factor of inheritance, in a disease like tuberculosis, may well be that since the course over a long period of time of tuberculosis in a community is that of a wave rising slowly at some time, stabilizing perhaps for a while and then falling gradually, is that the findings may be distinctly opposite according to whether the observer studies the situation in a group or country for instance, where the tuberculosis epidemic is evolving and increasing—as in Norway a generation ago, or in Puerto Rico now—compared with one—as in England, or among Jews—where it is declining. But it is primarily and only through tuberculosis itself that immunity is to be acquired: it is thus that racial differences have been attained. The process, however, need not be hazardous, slow and cruel; its dangers may be controlled, its favorable results accelerated.

**Sociological Factors.**—Under this group, to which only a reference can be made here, might be noted, apart from natural conditions that influence tuberculosis, certain environmental factors that nowadays are having perhaps a greater



play than ever against tuberculosis, especially in communities where active anti-tuberculosis campaigns have been evolved. Among these, especially in the United States, we should include pasteurization of milk and the consequent reduction therefore of opportunities for infection from that source of food so vital in childhood; likewise, the examination of food handlers in certain communities limits opportunities for transmission. Then, there are the far reaching popular campaigns for health education promoting general health and resistance; the registration of open foci of infection; and the vast system of tuberculosis dispensary services with home sanitary supervision of cases and their contacts. Finally, among all important, specific activities there is the extensive amount of institutional and sanatorium work. There are now in the United States nearly one hundred thousand tuberculosis beds available, through which, in a few years, literally hundreds of thousands go and are most practically educated in correct, hygienic living. Furthermore, there is being segregated therein an increasingly large proportion of all tuberculosis cases. For instance, as previously noted by the writer in the investigation of case fatality rates in tuberculosis<sup>69</sup> in the United States and England, during the 20-year period, 1915-1934, the proportion of all tuberculosis cases hospitalized rose here from 4 to 25 per cent; in England, between 1921 and 1934, the proportion of all cases institutionalized doubled, passing from 8 per cent of the total to 17 per cent. As the writer noted several years ago,<sup>70</sup> there is a distinct relation nowadays between the tuberculosis death rate in communities and the amount of institutional provision available for the care of the tuberculous. Lastly, and of general influence, are many improvements in sanitation, in housing, and in working and living conditions.

So powerful are all of these factors that in the United States, particularly during the recent economic depression, there has been a continued and, for that matter, accelerated gain against tuberculosis mortality. The death rate which in 1929 was 76 had fallen to 47 in 1939 or by more than 35 per cent in just ten years. Both naturally and by concerted efforts the control of tuberculosis is being achieved.

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## CHAPTER II.

# THE NEWER BIOLOGY OF THE TUBERCLE BACILLUS; ITS VARIABILITY, FILTRABILITY, AND LIFE CYCLE CHANGES.

RALPH R. MELLON.

### HISTORICAL AND GENERAL CONSIDERATIONS.

**Acid-Fast Bacteria.**—The tubercle bacillus was discovered and isolated by Koch in 1882, although the infectious nature of tuberculosis was strongly suspected by the interesting, if incomplete, experiments of Villemin in 1865, and of Baumgarten in 1882. The organism belongs to the group known as the acid-fast bacteria, because of their resistance to decolorization by mineral acids, when once they have been adequately stained by carbol fuchsin. This acid-fastness varies widely with different strains under different environmental conditions. But these differences often occur *willy nilly* and for that reason cannot be successfully employed to distinguish different members of the group.

Formerly attempts were made to distinguish the smegma bacillus from the true tubercle bacillus by these differences in acid-fastness, but such attempts have been largely abandoned. This interesting quality of acid-fastness has been pretty definitely correlated with the presence in the organism of a higher alcohol, rather than with its high lipoidal content. It is to the latter that the ordinary culture of tubercle bacillus owes its waxy, friable character and to which at one time the property of acid-fastness was supposed to be due; but it is now clear that cultures may be quite acid-fast which are as devoid of waxiness as is the ordinary nonacid-fast bacterium.

This characteristic from the diagnostic standpoint has been of very great importance because in any material suspected of being tuberculous it is only the acid-fast organisms that are sought out. Although it has been recognized that some bacilli in a culture of the tubercle bacillus were not always acid-fast under all conditions, there never has been any way on morphologic or staining grounds to differentiate such forms from other totally unrelated nonacid-fast species. Therefore, it has been impossible to utilize in a diagnostic way the many isolated observations that have been contributed to this aspect of the subject. And from the theoretical standpoint the significance of such forms has to a large extent escaped recognition, as will become clearer presently.

*Morphologically*, tubercle bacilli are rather slender, somewhat curved, non-motile rods, approximately  $0.3\ \mu$  in diameter and varying in length from  $1.5\ \mu$  to  $4\ \mu$ . They are usually arranged singly or in pairs, but sometimes are disposed in small or large groups, depending somewhat on the strain. The morphology and grouping also depend in no small degree upon the type of culture medium

employed. With unusual strains, or under exceptional conditions, branching or club-shaped forms may be observed. It was largely for this reason that Metchnikoff and the early observers felt that the organism was closely related to the actinomycetes; but today we know that the colon group, as well as some other groups of bacilli, shows no differences in this respect if the cultural conditions are suitable. The allocation is therefore called into serious question, the validity of which must necessarily be established by additional and more stringent criteria.

*Resistance Powers.*—Tubercle bacilli are apt to show greater resistance powers to unfavorable environmental influences than most other non-sporing bacteria. This is on account, presumably, of the protection given by the rather large amount of waxy substances which they contain. They may remain viable in water or sewage for some weeks, but for the most part they are not particularly resistant to drying, and are especially vulnerable to sunlight. Under some conditions they may resist dry heat at  $100^{\circ}\text{C}.$ ; but are usually killed at  $45^{\circ}\text{C}.$  On the other hand, they are quickly killed in fluid media, two minutes killing them at  $83^{\circ}\text{C}.$ , and one-half minute at  $95^{\circ}\text{C}.$

They are destroyed in sputum in six hours or less in the presence of an equal quantity of a 5 per cent. solution of carbolic acid. Bichloride of mercury is less effective under these conditions because it is precipitated by the albuminous substances in the sputum before it is able to reach the bacilli in the interior of the albuminous mass. It is noteworthy that the tubercle bacillus resists the action of alkaline hypochloride solution, antiformin, a solution which quickly dissolves bacteria which are nonacid-fast. Inasmuch as this reagent dissolves the exudate making up the sputum it has been employed to good advantage as a method for condensation of acid-fast bacilli when their sparsity would make detection difficult.

*Cultural Requirements.*—The more highly adapted or parasitic strains of tubercle bacilli are usually rather fastidious in their cultural requirements, growing only after some weeks. The best culture medium is an egg base to which glycerine is usually added in concentrations of 3 to 5 per cent. In order to restrain growth of nonacid-fast bacilli certain bacteriotropic dyes are often added. The ones in most familiar use are gentian violet, and malachite green.

As cultures lose their virulence or become adapted to artificial conditions the requirements for their cultivation *in vitro* are less exacting. For example, they may be grown on blood agar or on serum agar, often at temperatures which are not greatly above that of the room at  $30^{\circ}\text{C}.$  On bouillon or other liquid media the growth floats on the top of the liquid in pellicle form. With appropriate strains such growth may continue for weeks or months, building up finally a thick felted mat, very rugose in character.

It has been rather generally believed that virulent tubercle bacilli do not multiply in nature except in the animal body. Of course this has not been supposed to hold for many of the saprophytic acid-fast bacilli such as the well known timothy bacillus, which is found normally outside the animal body; and even when found inside their existence is a commensal one, never being known to have given rise to disease. But, it is generally held that all parasitic types

of bacteria represent adaptations of forms previously existent in nature in the wild or saprophytic state; but that such forms were capable of reverting to the harmless type, while still retaining the potentiality for re-adaptation under favorable conditions, is a conception which has not found favor. More especially is this so when this harmless type possessed cultural characters that seemed to place it in another species. However, the newer studies on variability have brought more clearly into view such possibilities, even though their occurrence at the present time is limited to the relatively artificial conditions of the test-tube.

An especially interesting consideration is the fact that these variation studies shed much light on the difficulties underlying the clean-cut separation of the several types of tubercle bacilli. There are, of course, the well recognized human, bovine, and avian types, in addition to the group affecting cold-blooded animals. In the order named these grade progressively toward the saprophytic acid-fasts found in nature, and generally speaking, the cultural characteristics of the latter on artificial media are by no means as fastidious as are the more highly adapted human and bovine types. In any type classification of bacteria it is always the intermediates that give trouble in their allocation. Particularly has this been the case in typing the tubercle bacillus because there has been no single character like the agglutination reaction, for example, that has proved sufficiently specific for the purpose.

*Variability.*—Despite the fact that the tubercle bacillus is one of the last to have attracted rather widespread interest from the standpoint of variability, it is becoming clearer that it is essentially no different in this respect than other microorganisms. Sometimes only single characters appear to be affected, while in other instances alteration of several has taken place. Thus it is rather easy to understand the differences occurring in individual strains whose characters sometimes may overlap to such an extent as to make type identification a matter of extreme difficulty. Although at the present time no convincing evidence has appeared to the effect that the well recognized type are intertransformable, or that the saprophytic acid-fasts may themselves be converted into one of the highly adaptative parasitic types, the possibilities from the experimental standpoint are more clearly thrown open for study than previously.

*In general* we may say that to date the accepted idea of the monomorphic character of the tubercle bacillus has prevailed; that it is an acid-fast rod, which invariably breeds true in this fashion alone and cannot be recognized with certainty in any other form. Moreover, there are certain definite cultural characters associated with this tinctorial character; and, although they may vary somewhat, this was viewed as of fleeting character, like the morphological variations of the bacillus itself.

## INTRODUCTION.

*Objective.*—To elaborate a point of view that in merest embryo was glimpsed several decades ago is one objective of this review. I refer to the well-known suggestion of Metchnikoff to the effect that the tubercle bacillus might represent an end stage in an evolutionary cycle. Its elaboration is only made possible by new experimental evidence of a critical character. Sufficient time

has not even elapsed to refine for others the conditions making for the success of experiments which are still under way.

But the results so far obtained integrate in such illuminating fashion the sum total almost, of fifty years' work on the biology of the tubercle bacillus, that in the writer's mind there is no reasonable doubt of their validity. Moreover, they harmonize perfectly with his twenty years' background of experiment in the variability and life cycles of other bacteria.

*Fact and Empiricism.*—It would, therefore, be ill fitting to the purposes of this discussion to confine it to matters on which there is unanimity of opinion. Moreover, I shall take the liberty of projecting the conception to situations, clinical and otherwise, where the evidence is as yet incomplete; which course sometimes is a stimulus to its completion or its rejection. But I shall attempt to separate clearly what is fact and what is the speculation of legitimate theory.

To withhold the latter would be to deny perhaps to certain receptive minds an opportunity to view diagnostic obscurities in the light of a new point of view; than which, in the writer's experience, there has been nothing more stimulating, not to say productive. Empirical, some will say—but it is of an order of empiricism which has had the approval of the practical clinician. For is it not true that legions of human beings would have been the losers had the therapeutic application of quinine, mercury, and cod-liver oil awaited our more precise knowledge of their *modus operandi*?

Admittedly, the latter is our goal, but mirage-like, it is one that ever recedes in proportion as we advance toward it. In its amplified vision and application we find compensation for this paradox. So after all, what is empirical and what is conceived for the moment to be scientifically proved are, in a measure, relative.

### VARIABILITY.

**Virulent and Avirulent Colonies; S and R Types.**—During the past decade a widespread interest has developed in a certain type of variability that involves the dissociation of smooth and rough colonies. Moreover, these are interconvertible. This interest takes origin chiefly, I believe, from the virulence correlations of these two types of colonies. Characteristically, but by no means invariably, the smooth or S type of colony is virulent, while the R or rough type is avirulent. Intermediate types, more or less stable, have also been shown to exist.

*Dissociation.*—As far as the acid-fast group is concerned Baerthlein<sup>2</sup> was the first to demonstrate that these two types of colonies existed among the acid-fast organisms. But he was not able to show their interchangeability, which came at a later time as the result of studies by Gildemeister.<sup>11</sup> These transformations were brought about by the simple and time honored measure of aging broth cultures and plating them out.

Gildemeister employed for his work the turtle tubercle bacillus, while Baerthlein and Toyoda<sup>3</sup> used the frog tubercle bacillus. But these studies apparently made no impression on workers in the tubercle field until it became clear that the majority, perhaps all, pathogenic microorganisms fall into this biphasic cate-



gory. Baerthlein,<sup>2</sup> Arkwright,<sup>1</sup> Griffith,<sup>12</sup> Hadley,<sup>13</sup> *et al.* More recently Petroff,<sup>27, 30</sup> Reed,<sup>33, 34</sup> and others, extended these observations to the avian and bovine tubercle bacilli. The technical procedures followed are those in general which have been found effective with other organisms; although at times modifications in accordance with the nature of the specific organism must be introduced.

In addition to aging—perhaps the one most effective procedure—we have serial transplantations in broth followed by plating on one of the standard media. Then again, the addition of an homologous antiserum, coupled in some instances with a diminishing ratio between the size of the inoculum and the nutrient, has

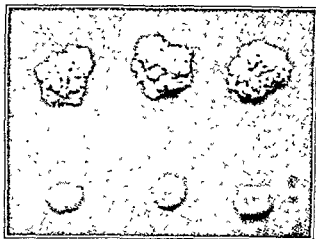


Fig. 1.—S and R forms of tuberculosis colony. The larger, irregularly shaped colonies are of an extreme R type (our critical R). The three smaller colonies are S in type.

also proved efficacious. Reed<sup>35</sup> has recently observed that the presence of killed homologous organisms tends to inhibit the growth of this type, but to encourage dissociation of the opposite type. This procedure had become particularly well established by workers in the field of pneumococcus dissociation.

Applying these various procedures singly or in combination, they have been able to transform smooth virulent colonies into rough colonies, either avirulent or possessed of but slight virulence. Also, the procedure has been reversed. The R colonies, so-called, are also characterized by their ready flocculability in salt solutions, while the S type form much more stable emulsions. Correlated too with these characters are, as might be expected, corresponding differences in electrical charge, and in cohesiveness. Instead of adhering too closely to the designation of smooth and rough, it has seemed best to the workers in this field to follow Petroff's idea, who thinks of the S type as representing sensitiveness to environmental dissociation, and the R type as more resistant to the influence of environmental change.

**Deductions.**—From this it is clear that the R type is the more stable and, of course, the more saprophytic; while the parasitic S is more labile, depending perhaps on the degree of adaptation which it has undergone in the host. It

should be realized, of course, that there are intergrades of these S and R colonies; particularly between their extreme representatives. Even the different colonies in an identical R culture may vary quite widely in their susceptibility to transformation by environmental change, and to a lesser degree the same thing is true for the S colonies. And we shall see in our experiments dealing with cyclic aspects of their variability that both S and R forms may shade imperceptibly into stages of the cycle hitherto undemonstrated; or at least unidentified with the acid-fast cause of tuberculosis. It is important to realize that the terms R or S do not adequately characterize strains of organisms; for they may contain other modifying factors that affect the stability of their R or S characters. This is another way of saying that R's and S's may vary markedly among themselves.

An aspect of this situation particularly pertinent at the present time has to do with the virulence potentialities of Calmette's BCG vaccine. Inasmuch as this vaccine is administered therapeutically in living form by way of the gastrointestinal tract, it is obviously a matter of practical importance whether the virus—so to speak—is permanently fixed in an avirulent condition, or whether it may revert, as is the case of other avirulent tubercle strains. In other words, is the BCG organism identifiable as one of the R forms of the bovine tubercle bacillus?

Although unanimity of opinion on this subject can scarcely be said to prevail as yet, investigations of Petroff and others in this field indicate with considerable certainty that there are several ways in which cultures of BCG can be made to dissociate the virulent or S form of the organism. This reversion is brought about not only in the animal body, but also by *in vitro* methods. Originally a virulent organism, this particular strain had been cultivated by Calmette and Guérin for many years on a medium made up of potato and ox bile. One of the important points in this connection is the fact that an acid environment restricts the growth of S colonies, but encourages that of the R form. Accordingly, Petroff believes that his potato-bile medium has effected an artificial selection of the R form at the expense of the S, which the low pH has largely suppressed. With his data at hand, this conclusion seems a reasonable expectation. Moreover, in its light, variations in virulence of such a supposedly standard strain as BCG become intelligible. It should be more clearly recognized indeed that the "standards of purity" for bacterial cultures are not strictly comparable with those obtaining for an inert chemical compound. Their biologic heterogeneity, resulting from variability changes, renders this impossible.

When in addition to such variables one takes into consideration the matter of dosage, the route of inoculation, the individual susceptibility of the animal or of the species, it is not particularly surprising that different investigators are not at the moment unanimous in their opinions. Moreover, there is the question of spontaneous tuberculosis in experimental animals, which there is a tendency to invoke when the percentage of positive infections is very low.

It is my opinion that sufficient evidence has accumulated and of a character that we may regard as formidable that the BCG strain cannot be regarded as a "fixed virus," but is susceptible like all other organisms of undergoing

variation in one or more directions; as the result of which it is entirely possible that its virulence may be regained. But this will depend on the stability of the particular R strain under consideration and the nature of the environment brought to bear on it. But as to the therapeutic value of this culture in its living form I believe that final judgment must come, not from what we know of the culture's potentialities *in vitro* or by *in vivo* inoculations, but under the conditions of the therapeutic experiment itself. That is to say, if it remain fixed in the human host, test-tube possibilities become academic in their significance.

**Conclusions.**—When it is considered that this illuminating type of dissociation which later was so clearly to involve virulence, was first described in 1895 by Dyar,<sup>8</sup> some idea can be gained of the thralldom in which bacteriologists have been held by the doctrine of *fixity of morphologic types*. Even as late as 1916 Cole and Wright<sup>4</sup> in a critical analysis of variability data came to the conclusion that up to that time there was scarcely a well authenticated instance of true variability that was not explicable as the result of the selective influence of special environments. They included, too, in their analysis Dyar's work, who himself partially succumbed to the then prevalent view, and in the end unfortunately, rather came to doubt the validity of his own results. Thus it was only natural for Calmette to believe that he had obtained a saprophytic form of the tubercle bacillus incapable of regaining its virulence.

**Filtrability and Life Cycle Changes.**—During the past decade controversy has arisen regarding the question of the filtrability of the tubercle bacillus. The real question at issue is not whether the typical acid-fast bacillus of Koch is capable of passing clay filters; but whether the organism gives rise to more minute and perhaps invisible forms that *are* capable of doing so. It is well understood, of course, that practically all species of bacteria are incapable of passing the pores of the finest filters, and in this respect they differ from the true viruses, all of which are ready filter-passers.

It is for this reason, perhaps, that Calmette and the French school have designated the filtrable phase in the life history of the tubercle bacillus as its ultravirus stage. In some respects the choice of the term is unfortunate, because of a tendency on the part of some workers to identify filtrable phases of bacteria with true ultraviruses. At the present time I do not believe there is any conclusive experimental basis for such a position; and until some such develops, it is perhaps as well to avoid the use of terms which, in themselves perfectly proper, are liable to confuse important issues.

The French point of view has been supported by a steadily increasing stream of publications since the initial work of Vaudremer in 1923,<sup>41</sup> the evidence for which can be condensed as follows: First, that the tissue products of tuberculous disease contain an invisible form of the organism capable of passage through Chamberland L-2 and L-3 porcelain filters. Although these filtrates, even when centrifuged, yield no morphologic evidence of the tubercle bacillus or its granular products, when injected into guinea-pigs there is produced an enlargement of the lymph glands often associated with a marked degree of cachexia. These lymph glands when examined at the proper time show acid-fast granules, very frequently acid-fast bacilli; but they are not susceptible of

cultivation on the conventional media. Nor are they capable of giving rise to progressive tuberculosis when injected into other animals. Serial passage, however, does occasionally result in the production of a caseous nodule from which the Koch bacillus can sometimes be isolated.

Usually the lesions in the lymph glands and organs are distinctly not those of tuberculosis of the classical type. It is claimed, in addition, that the animals injected with these filtrates may show a tuberculin reaction by the intracutaneous route and also when reinoculated sometime later may show the Koch phenomenon (local allergy). The basic elements of this work are essentially a confirmation of the original observation of Fontes in 1910.<sup>10</sup>

Unfortunately, Fontes is very frequently quoted as having demonstrated a filtrable form of the tubercle bacillus, but if one reads his original paper, this so-called demonstration did not carry him beyond the point where the injection of the filtrate resulted in enlarged lymph glands and the presence of a few acid-fast bacilli and granules. Such evidence is, of course, entirely too meagre on which to rest a case of such possible significance. Even with the additional observations and the repeated confirmations of the French school, the evidence is still unacceptable to many as conclusive proof for the claims made.

*Objections.*—The objections are numerous, but I shall refer to but two of them. In the first place comes the question of filtrability technic. It is claimed by the opponents of the view that the percentage of positive results is just about covered by the per cent. of experimental error in connection with this technic. That is to say, that in certain instances a few normal bacillary forms of the tubercle bacillus may slip through the filter, and in the occasional case where actual tubercle lesions appear their presence becomes intelligible on these grounds. The French proponents, of course, believe that the clinical-anatomical picture produced is in itself a special and anomalous form of tuberculosis which has hitherto been unrecognizable.

The second objection has to do with the nature of the acid-fast bacilli and granules which are found in the glands following the injections of the filtrate. If these are true tubercle bacilli, it is not clear to the average worker why they are not cultivable on the conventional media, even granting that their virulence may be impaired. And in the latter event, even with cultivation successful it is not clear why on serial reinoculation into animals that the classical type of tuberculosis is not produced. Of course, if the passages are through a large enough series of animals, this occasionally happens in a rather modified form, but the opponents are inclined to explain such an infrequent result as a spontaneous tuberculosis. In any event, the percentage of positive results, even under the best conditions, is quite too low to clear away the doubt in their minds; particularly when it is reinforced by equally pertinent doubts regarding other aspects of the contention.

*Results.*—In a last analysis categorical results can only be obtained from a study of pure cultures; for it is a fundamental weakness of the whole work that animals must be so consistently employed with all the hazards that they involve by way of spontaneous infection, secondary infections, contaminations, etc. Indeed, the fact that virulence and pathology loom so important as *criteria for*

the demonstration of filtrable forms, in face of their relatively avirulent character and the nondescript pathology elicited by them, leaves the situation a bit at a disadvantage. This together with the fact that the acid-fast bacilli when found, are few at best, their presence usually transient, and their cultivation very difficult, relieves the situation not at all. Even when cultivable, their transplantation in series has not proved feasible and their inoculation into animals still does not result in the production of tuberculosis. Under certain conditions, however, the rabbits die rather quickly with curious paralytic symptoms. Altogether, this may be said to summarize briefly the situation, particularly on the more important of those points to which its opponents have taken exception.

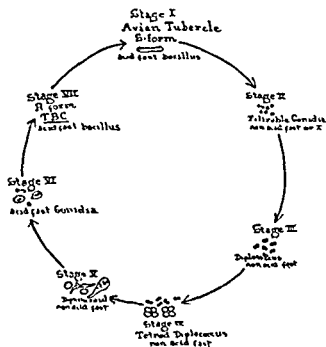


Diagram I.—The Avian Cycle.

**New Experiments With Pure Cultures of Tubercle Bacilli.**—I shall now recount some of the high lights of our own experiments dealing with the production of a true life cycle for the avian tubercle bacillus. For the experimental details of this work as they have been published so far the reader is referred to our previously published papers on the subject.<sup>21, 22</sup>

From the above diagram it appears that Stage I represents the well known, normal, acid-fast avian tubercle bacillus. This organism grows in smooth colonies, the so-called S form, and is possessed of characteristic virulence. It is from it that the filtrable stage represented as Stage II is developed. This has been made possible by the special environmental conditions of a new medium for the details of which the reader is referred to a recent paper.<sup>23</sup> To our knowledge this is the only method described by which it has been possible to reproduce this filtrable form of the organism in the test-tube with a reasonable degree of certainty.

It might be imagined that once this has been accomplished the rest is easy, as far as demonstration of the cycle is concerned. But as a matter of fact such is far from the case. One is immediately confronted with the difficulty of bringing about germination of these filtrates; for they are possessed of remarkable dormancy very much like that present in bulbs of the higher plants, or even the potato. The latter, for example, would not germinate if, after harvesting, it were immediately put back in the ground, even under favorable conditions. Before it is capable of sprouting, a long latent period must elapse, or failing in this, special environment must be induced to break this dormancy, so to speak.

*Germination Induced.*—And the situation with regard to the germination of these filtrates is similar. Suffice it to say that in a very fair percentage of cases their dormancy has been broken and germination induced. But it is very remarkable that the latter event brings about results that would be totally unexpected, if one were not familiar with the biologic potentialities of the situation. For instead of germinating into the original tubercle bacillus from which they came, they appear first as tiny granules or diplococci, represented as Stage III in the Diagram. This *nonacid-fast diplococcus under special conditions may give rise to pleomorphic forms in the shape of large tetrads which are associated with the transition of the diplococcus to the next stage in the cycle represented in the Diagram as Stage V.*

It is to be remembered now that this diplococcus, Stage III, is a saprophytic form capable of reproducing itself on ordinary media and at ordinary temperatures indefinitely, and would be recognized by conventional bacteriology as a separate species, entirely distinct from the tubercle bacillus from which it came, as well as from Stage V into which it is capable of progressing. For the latter organism is not a diplococcus at all, but a *pleomorphic, granular bacillus, indistinguishable in its morphology from a great many of diphtheria-like bacilli, or diphtheroids.*

In the mind of the average worker such strains have always been attributed to contamination, but so far as our own observations are concerned, we are in a position to show that such interpretation is erroneous. The crux of the whole matter becomes very evident, upon the observation that these *nonacid-fast diphtheroid forms are capable of progressing into Stage VII, which culturally and in every other way, except virulence, is a tubercle bacillus.* But its colonies in contradistinction to the S or smooth form from which the cycle started are very rugose or shaggy. That they represent one of the extreme rough or R colony forms of the tubercle bacillus has been conclusively proved by forcing them to revert in the test-tube to the original or S form with which the cycle started. Moreover, this S form is now possessed of typical virulence and the serological characteristics of the avian organism. Thus the cycle has been completed and entirely *without resorting to the experimental animal at any stage.*

Moreover, this cycle embraces what conventional or monomorphic bacteriology would regard as several distinct species, entirely unrelated to the tubercle bacillus as we know it. This all means, of course, that such species designations can scarcely be considered comparable to that obtaining with higher

plants. For the benefit, too, of those who are critically inclined, it may be added that as an additional protection against contamination or mixture in our cultures, these different species (?) have been repeatedly isolated from the single bacterial cell before bringing about their progression to the next stage in the cycle.

*Recapitulation.*—In reply to those who are suspicious of filtration technic (see Zinsser<sup>44</sup>) suffice it to say that identical results have been secured *without the employment of a filter*. To those who would regard the nonacid-fast forms

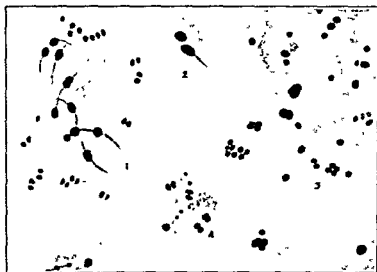


Fig. 2.—True sporoid granules of the tubercle bacillus. (According to Swamy.) The bacillary connecting portions are acid-fast, while the coccoidal portions vary from faint magenta to bluish black. Note under (2) how the sporoid portion has appeared to grow at the expense of the bacillus. Note contrast in mechanism of granular formation with following figure.

derived from filtrates as contaminants, suffice it to say that they are capable of returning to the original acid-fast form, which obviously would not be true for contaminants. And for those to whom the employment of the experimental animal is an objection, our reply is that we have used none for the demonstration. This would seem to remove the legitimate objections so far raised.

*Calmette's Ultravirus.*—One of the very curious things about these filtrates is that they contain no demonstrable acid-fast tubercle bacilli when they are properly prepared. It seems rather paradoxical therefore, that anything should be cultivated from them, or that they should produce results in animals that should in any way suggest tuberculosis. Their invisible character formed an additional reason why Calmette was inclined to speak of them as an ultravirus. But apart from the character of filtrability which they have in common with our own filtrates it is not possible to say with finality how much our findings have in common with the French work. It is enough to say that there are a number of important points at which they are in contact, but that this number will have to be considerably increased by additional work, if it can be ultimately

concluded that their tubercle ultravirus is identical with what we are pleased to speak of as our "filtrable gonidia."

By the term "gonidium" we mean a granule or other pleomorphic form having reproductive significance, in contrast to the purely vegetative manner in which the normal form multiplies, namely, by transverse fission. By the latter method the acid-fast bacillus may be transplanted almost indefinitely without significant variation; but from the granular form, as we have seen, there develops a totally different stage in the life history of the culture. This is a characteristic mark of reproductive forms.

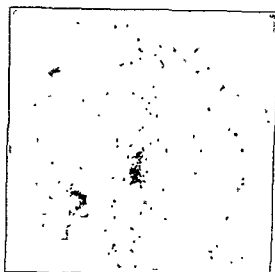


Fig. 3.—Bacilli segmenting into filtrable nonacid-fast free granules. The rods appear to form segments which have fission lines resulting in minute coccoid forms, single and diplo. Comparable with Kahn's warm stage studies. X 1000.

The best known granule form of the tubercle bacillus is the one which goes classically under the name of Much. It will be recalled that Much granules vary greatly in size, but are characterized particularly by the fact that they are nonacid-fast and Gram positive. As a matter of fact, they were repeatedly described and very well known long before Much's name became associated with them. From a study of our cultures which we subject to filtration it seems likely that these granules of Much or similar structures biologically their equivalent are the ones that pass the filter, although for technical reasons their presence there is very difficult to demonstrate with certainty.

Indeed the fact that they often germinate first in the form of nonacid-fast granules makes it probable that their germination is from nonacid-fast granules such as Much's, particularly when no acid-fast structures can be recognized in the filtrate. It would seem likely, too, as we have recently pointed out,<sup>20</sup> that the nonacid-fast forms of the tubercle bacillus which have been known for so long a time to occur spontaneously in the cultures, take their origin from these granules.



## CLINICAL SIGNIFICANCE OF NONACID-FAST FORMS.

It has been known for a great many years that the youngest forms of a tubercle bacillus culture were nonacid-fast, preliminary to their becoming acid-fast. This is, of course, a different matter from our position, which says that certain nonacid-fast forms may reproduce themselves indefinitely as totally different species before ultimately returning to the classical bacillus of Koch. But fundamentally the two positions have more in common than at first appears, although it is not feasible to discuss the details in a presentation of this sort. I might add that for detailed treatment of this and other related fundamental questions on the biology of this cycle I must refer the reader to a more technical monograph now in course of preparation. In any event, the point of most interest at present is an extrication of such forms from their academic hideout to see whether they have anything of practical bearing.

As an extension and verification of the work of Wolbach,<sup>43</sup> Dreyer<sup>7</sup> has made interesting observations of the nonacid-fast phase of the tubercle bacillus, particularly in connection with its virulence and infectivity in experimental animals. Whereas the tubercle bacillus conventionally grows in scum or pellicle form on the surface of broth, he forces it to grow in the depth of the medium. In this manner he obtains his nonacid-fast or chromophobic stage, so-called. It is of special interest in these experiments that certain of the guinea-pigs die in the acute phase of the infection, showing no visible tuberculous lesions. But those that survive are reasonably apt to develop typical lesions at a later time, while some of the inoculated animals develop no lesions whatever. In other words, depending on their susceptibility, the animals may die of acute sepsis without lesions, or may run a more prolonged course, finally developing typical lesions, or they may survive for years with slight, but innocuous, lesions.

The importance which Dreyer attributes to the nonacid-fast chromophobic forms was previously affirmed by Sweany<sup>39</sup> as the result of his clinical and experimental observations. They bring clearly into view the fact that if the nonacid-fast forms are not so far removed from the normal acid-fast ones as to become entirely saprophytic, that they give rise to very acute septic-like lesions, in which characteristic tuberculogenic properties are at first entirely lacking.

Moreover, the clinical and pathological features of this type of inflammation are indistinguishable in its acute stages from that caused by other varieties of pyogenic organisms, and it is only in the event that the acute phase subsides that the more classical symptoms and lesions may develop. These epituberculous infections, so-called, are recognized as being anomalous cases of tuberculosis. Normally such of these nonacid-fast variants as possess virulence very likely enter into the tuberculous process as *secondary infections*, but they may play the dominant role in certain meningitic types, typhoid types, and other unusual variations of the disease.

LANDOUZY'S "TYPHOBACILLOSIS" AND ITS  
CYCLIC CONNOTATIONS.

**Secondary Infections.**—Entirely in line with these observations are the classical ones of Landouzy,<sup>14</sup> recognized theoretically but so often overlooked clinically. With what must have been a rare clinical perspicacity and at a time when we were just beginning to know about the tubercle bacillus and the typhoid bacillus, he distinguished on purely clinical-anatomical grounds an aspect of tuberculosis which he refers to as typhobacillosis. "Symptomatically, this is an acute infection resembling enteric fever, rarely fatal in the acute stage, but some time after an apparent recovery the patient develops well-defined typical tuberculosis of some organ. If death occurs in the acute stage no typical localized tuberculous lesions are found, but only the diffuse congestion and degeneration common to all acute septicemias."<sup>17</sup>

**CASE I.**—I shall now illustrate concretely certain variations of this situation by clinical observations from my own experience. The first case was that of a young girl who had received a rather severe sacroiliac sprain and general shaking up in an automobile accident. Her slow recovery from the immediate consequences of the injury was followed by the development of a continuous fever. It later took on the intermittent or septic type with fairly wide swings and lasted for a number of months, with the diagnosis quite shrouded in obscurity.

A diffuse and general haziness of a thoracic x-ray plate left nothing definitive on which to base a diagnosis, but proved significant in light of the later developments. There was repeatedly isolated from the blood a Gram amphotrophic, somewhat granular, type of organism having a diphtheroid-streptococcus morphology. But the pleomorphic aspects of the blood culture were such as to suggest a pulmonary case presenting similar diagnostic difficulties reported by the writer many years ago as a streptothricosis of the lungs.<sup>18</sup>

In such cases it should be remembered that potassium iodide has the two-fold advantage of bringing up a sputum for diagnosis while benefiting the case therapeutically if active tuberculosis be absent. I might say that both of these happy eventualities took place in this case, the patient's temperature returning within seventy-two hours to normal; and a sputum was raised which contained numerous small spherules, comparable in a general way to the little caseous masses of tuberculosis, yet far from identical in appearance. In my 1919 paper<sup>18</sup> I have stressed the importance of the structures in a diagnostic way, but I have no doubt that they are usually overlooked, or misinterpreted, even if sputum be present. The mucopurulent exudate containing these particles revealed in almost pure culture the same type of organism as was present in the blood culture.

**Treatment.**—Under the influence of iodide and good hygiene the patient made a perfect recovery, only to develop within two years a typical pulmonary tuberculosis! Whether there were contributing factors in her breakdown I have never learned. Although it is probable that this sequence of facts would not be interpreted the same way by different observers, it is at least suggestive as a clinical reflection of the wide arc through which the tubercle bacillus may be conceived to swing.

The paramount point here is, of course, that we have a bi-phasic condition clinically. The first or septic phase can scarcely be distinguished from typhoid fever; but in the second phase some form or other of classical tuberculosis develops, usually severe and often fulminating. Separating these phases is a convalescent or relatively afebrile period, whose length varies from a few weeks to months, or even a year or more, depending somewhat on the individual case.

The series of events in the above case coincide so well with Landouzy's description that I believe that we must regard it as such. But it is of particular interest that the various nonacid-fast organisms that may be found in the blood of these cases during the septic stage may represent nonacid-fast cyclo-stages of the tubercle bacillus. In fact, to link up the cyclic activities of the organism with the clinical picture we need but to assume the presence in the host of our critical *R form* (Stage VII, Diagram I) of the tubercle bacillus. We have so named it because it is capable of dissociation *in vitro* in either of two directions; namely, to the *S acid-fast form*, or to a Gram negative nonacid-fast bacillus. One of the latter causes acute sepsis in rabbits, while the *S form* causes classical tuberculosis.

Now, if such dissociations occurred *in vivo*, first of the nonacid-fast form, and at a later period of the *S form*, the bi-phasic clinical picture could conceivably result. Immunity to the nonacid-fast might well result in change in the reaction of the host that would favor dissociation of the virulent acid-fast form. Similar contrasting immunologic and susceptibility relationships are already known to occur in tuberculosis.

There is a noteworthy tendency on the part of the French school at the present time to explain this situation by what Calmette refers to as the prebacillary granulemia. In other words, it is their belief that it is the ultravirus or granular phase of the tubercle bacillus which gives rise to the sepsis and that this then develops into the normal tubercle bacillus. Such a view, although entirely possible, is not very susceptible of proof inasmuch as it is not possible to cultivate this ultravirus stage as such. And when it does grow, the cultivation results of Ninni<sup>24</sup> showed that it germinates into rather stabilized nonacid-fast forms, such indeed as may be isolated from these cases in lieu of the normal tubercle bacillus; and which monomorphic bacteriology would, of course, regard as contaminations or secondary infections. Löwenstein<sup>14</sup> on the other hand with his special blood culture methods and the frequency with which he finds tubercle bacilli in the blood, would attribute this condition to a tuberculosis bacillemia which simply precedes localization.

But the assumption that one is able to cultivate the tubercle bacillus from the blood of such cases by special technic is not in itself proof that the organism is present there in that particular form. The experimental results of Dreyer<sup>7</sup> show that one may obtain a nonacid-fast, but readily reversible organism under special conditions of cultivation which gives the impression at times of being much more virulent than the acid-fast form.

From the standpoint of secondary infections, so-called, in tuberculosis such a correlation indicates that a reversal in the usual order may occur. That is to say, the pyogenic factor may present first, in lieu of full virulence and adapta-

tion of the infecting tubercle bacillus. The one obvious expectation with reference to the blood culture findings in this condition would be a diversity, somewhat comparable to that shown in the *nonacid-fast* progeny of the tubercle bacillus itself.

CASE II.—I shall now relate a case somewhat similar to the above in which a Gram negative member of the enteric (?) group was repeatedly isolated from the blood. A low-grade fever occurring in a middle-aged man directly after his return from a vacation in the mountains and associated with marked enteric symptoms suggested, of course, that he had acquired typhoid fever. But serologic tests for members of this group proved quite negative. The fact that for many years he had carried a displaced kidney, but one which had become harmlessly anchored in the pelvis, rather diverted attention to this as a possible source for the symptoms. An exploratory abdominal operation had only one noteworthy effect and it was entirely unsuspected; the temperature, which up to that time had been mounting for some weeks, disappeared quite abruptly, as one often observes after operation on tuberculous ascites.

For some weeks the patient was afebrile, but he then developed a psoas spasm which finally became so marked as to be rather obvious. His fever again started to rise and following a second operation on the suspected kidney the patient died in surgical shock. Even though the writer was not connected with this case in any intimate capacity, as he reviews the circumstances in connection with it, it seems probable that it was an undiagnosed tuberculosis of the spine. Many physicians and consultants saw this case—for the patient was a physician himself—but there was never, as far as I am aware, any suspicion of tuberculosis entertained.

A Gram negative bacillus of the enteric group was repeatedly isolated from the blood, which comes to mind in its possible relation to the dissociation of Gram negative types from the tubercle bacillus.<sup>38, 40</sup> The case raises the question at least whether one may invariably expect to isolate the normal tubercle bacillus from the blood in "typhobacillosis." Moreover, when the tissue reactions and the serology are often as anomalous as the clinical picture, is it not permissible to think of all these as possible reflections of marked biological changes in the parasite itself?

#### TUBERCLE BACILLUS IN THE BLOOD.

It has only been within recent years that the question of the tubercle bacillus in the blood has come to the fore to any great extent. For a long time, of course, it has been recognized that through the accident of a tubercle rupturing into a vein that a widespread dissemination of tubercle bacilli in the blood stream would then result in a generalized miliary tuberculosis. In less dramatic situations it was still regarded as probable that at times the tubercle bacillus found its way into the blood stream, but this was largely a matter of inference from attendant circumstances rather than the result of direct culture of the blood. But, on the whole, this question has been viewed rather negatively.

**New Views.**—During recent years Löwenstein has made some new and startling announcements quite the antithesis of the older beliefs. In his 1930 paper<sup>15</sup> he indicates that he obtained positive blood cultures from 169 out of 325 cases, that is 52 per cent.; and his series included tuberculosis of the lungs, skin, larynx, kidney, bones, and eyes, and also twenty-one cases of acute rheumatism, all of which gave positive evidence.

Löwenstein believes that there is little doubt that the bones, the eyes, the kidneys, and the skin become infected with tuberculosis through hematogenous paths. A search by the very best technic often does not yield any evidence of an original focus in the lungs. But a review of the large number of autopsies also shows that in 60 per cent. of the cases of bone tuberculosis, 40 per cent. of urogenital tuberculosis, the protocols show no foci of tuberculosis. Orth<sup>20</sup> came to similar percentages in bone tuberculosis series. Löwenstein in referring to his initial demonstration of avian tuberculosis in man in 1913<sup>16</sup> says that such cases behaved themselves as ones of outspoken bacteremia; but they were characterized during the course of a month to a year with a low-grade fever, with a low morning and evening temperature—38.5° C., but in which visible localization only occurred at a later time.

Löwenstein believes that the bacillemia occurs much earlier than the tuberculin reaction and that it conditions the development of the latter. And this for the following reasons: in the first place he believes that a pure tuberculin hypersensitivity is brought about only with living tubercle bacilli, and that the tubercle hypersensitive cell must enter into reaction with the living tubercle bacillus. Moreover, when once the organism is hypersensitive, not only the skin, but the subcutaneous tissues, the bones, the mucous membranes, and even connective tissues are hypersensitive.

He also believes that it is not necessary for the patient to have fever in order to have tubercle bacilli in the circulating blood. For example, in fever-free cavernous cases which he has encountered during the past decade, the bacilli have been demonstrated in the blood in 80 per cent., in spite of the relatively good condition of the patient and a negative sputum. With progressive tuberculosis the percentage reaches between eighty and ninety. Even in a condition like lupus erythematosus the tubercle bacillemia persisted as long as the disease was acute, disappearing only with recession of the symptoms.

In another section I shall speak of the experimental production of tissue reactions so anomalous as to be unrecognizable as tuberculosis, even with our present standards of what constitutes the atypical. Of these extrapulmonary types of infection in which Löwenstein finds the organisms in the blood he makes mention of the fact that the tissue reaction is apt to be very weak and quite non-specific. It is interesting in this connection to recall the fact that the tissue changes caused by the tubercle bacillus are so inconstant and so protean that even Virchow himself for a long time doubted that the tuberculosis of cattle was caused essentially by this organism. It is a classic, of course, that Virchow could not bring himself to align all the pathological manifestations under one single cause, even in face of Robert Koch's convincing experimental demonstration.

*Skepticism.*—Striking as are the observations of Löwenstein with undoubted cases of tuberculosis, their extension to certain other types of cases whose tuberculous origin is often entirely unsuspected has given rise to much wonderment—not to say, frank skepticism. Nevertheless, it is illuminating that in Poncet's disease—the so-called polyarthritis of children—its suggestive tuberculous symptomatology has been reinforced by finding tubercle organisms in the blood stream. Reitter<sup>36</sup> particularly has shown that tuberculosis in its secondary stage is a conspicuous factor in the development of the symptom complex of many of the polyarthritides; but especially of acute polyarthritis; and he has made staining demonstrations of tubercle bacilli from the joint punctures. Reitter shows in twenty-two out of twenty-seven cases of rheumatism, in which there is acute polyarthritis, that tubercle bacilli have been demonstrated at the height of the joint inflammation. Following the periods of remission the organisms were no longer demonstrable, which suggests to him that there is a large field of acute and subacute rheumatic joint diseases which show their inflammatory complications related to tuberculosis.

It seems strangely paradoxical to associate the tubercle bacillus with conditions that hitherto have yielded the diphtheroid and streptococcus groups as their chief bacterial flora. Until the validity of this finding is put beyond question it would be premature to draw conclusions of any sort. But in the re-study of such cases that is under way there can certainly be no harm in a simultaneous reconsideration of the pertinent nonacid-fast flora as possible progeny of the tubercle bacillus. This along lines already discussed under secondary infections and typhobacillosis.

Additional impetus is afforded to such attempts by the curious fact that this group of patients gives a high per cent. of complement fixation reactions with tuberculosis antigen. (See chapter on Diagnosis of Tuberculosis by Laboratory Tests.) Moreover, diphtheria bacilli and diphtheroids absorb tuberculosis antibodies which in light of the cycle relation between the forms (Diagram I) might offer plausible explanation. And there can be no reasonable doubt of the inter-transformability of streptococci and certain diphtheroids as we have shown repeatedly<sup>17</sup> and for which there is now substantial confirmation.<sup>32</sup>

*Possibilities*—The point of importance is that we follow Darwin's original injunction as follows: "The great point is to give up the immutability of specific forms." In other words, our idea of what constitutes specificity in the microbic causes of disease must be broadened to include, where indicated, the cyclic connotations of such causes. In awaiting further developments, we may at least preserve an open mind until conclusions can sensibly be drawn.

And these, it must be admitted, are made more difficult by Löwenstein's isolation of tubercle bacilli from the blood of such cases as chorea rheumatica, spinal meningitis, and dementia præcox, and similar conditions. He raises the possibility that certain mental diseases are not always luetic as they have been supposed, but they may in the last analysis have a tuberculous base. Still more wonderment is occasioned in connection with the studies of Wagner who in certain of these cases had employed infinitesimal doses of tuberculin with favorable clinical results.

There have been some attempts at repetition of Löwenstein's blood culture studies, both in tuberculosis and other diseases. In personal conversation with those engaged in this work, as well as reports that have come to my attention in the literature, there has been a noteworthy lack of confirmation without which the general acceptance must remain *sub judice*. A notable exception in experimental animals occurs, however, in the recent studies of Dreyer and Vollum.<sup>7</sup> Their experiments direct our attention pointedly to the conclusion that a rapidly developing fatal tuberculous septicemia is more common than is usually recognized.

**Blood Cultures.**—In some 152 guinea-pigs, including controls and unsuccessfully vaccinated animals, they obtained positive blood cultures in 91 per cent. The incidence was highest in the acutely infected animals. These results appear to depend in part on an almost unsuspected variation in susceptibility of the guinea-pigs employed. In a single experiment some survived for years with but slight or negligible lesions. A certain proportion died in the ordinary period of time with typical lesions, but a number died of an acute sepsis caused apparently by tubercle bacilli; for no other organism or no other cause for the sepsis could be found.

It is his chromophobic or nonacid-fast stage which he is strongly inclined to believe multiplies for a certain time in the blood stream; but which on isolation is capable of growing out into typical bacilli of Koch. On this basis he would account for the marked discrepancy between the number of acid-fast organisms observed in the blood itself and the cultures from it. Moreover, he takes the point of view "that it is probably generally accepted that in clinical and experimental tuberculosis, bacillema occurs in some stage of the infection, but the question of when it begins and how long it persists is still unsettled." He even goes so far as to relegate the tubercle bacillus of Koch's classic description to a comparatively minor place in the pathogenesis of tuberculosis. "It appears to be a resting stage of the organism, and possibly its least active form."

But for the moment the confirmation of positive blood cultures in clinical tuberculosis are comparatively rare. Numerous observers have reported either negative results or simply an occasional result. Norton, too,<sup>25</sup> in a recent study has attempted to get an estimate of the number of tubercle bacilli which must be present per cubic centimeter of blood in order to secure successful isolation. The impression was given when he read his recent paper that under experimental conditions, one in order to re-isolate from the blood must inoculate with more organisms (50 to 100 per c.c.) than it seemed reasonable to think might enter it under natural conditions.

If reconciliation between these widely divergent opinions be destined to come about, it is just possible that it will be made on the presence in the blood stream of an anomalous and probably nonacid-fast phase of the organism. I know full well that some of our filtrates from which we are able by special methods to obtain both the tubercle bacillus and the acid-fast diphtheroid variant often fail to yield them when they are transplanted to any of the conventional media for the purpose.

Such a suggestion recalls the view of Calmette on a pre-bacillary stage being in the blood, or that of Dreyer on the chromophobic, nonacid-fast stage. On the other hand, Lowenstein uses a medium of known composition presumably, so there must be technical difficulties involved which are not clearly understood at the present time. This may be inferred from the study of Deist<sup>6</sup> who after repeated blood culture failures (three positives in 287 cultures), took the position that if the organism was present in the blood it might also be present in the urine. He was able to verify this hypothesis by the isolation of the tubercle bacillus from the urine in twenty-three out of fifty-nine cases. That this was due to a permeability of the kidney for the organism and not to any focus or lesion in the kidney itself, was clearly verified by the autopsy findings. Moreover, he found that organisms were particularly apt to be liberated in the urine after such disturbances in the patient's physiological equilibrium as are occasioned by surgical procedures.

#### ATYPICAL TUBERCLE BACILLI AND ATYPICAL PATHOLOGICAL RESPONSES.

**Life Cycle.**—The life cycle of the tubercle bacillus as now developed makes possible for the first time the correlation of isolated observations that have accumulated for decades. The granules of Much, for example, were known in Koch's time and the nonacid-fast forms have also been well recognized. Even the S and R forms were described ten years ago, but only recently has their significance been appreciated. The fact that the sum total of these observations can now be allocated in a progressive sequence and cycle opens new possibilities for their clinical application.

For example, if in years past one were to have isolated from human lesions the R form of the tubercle bacillus, lacking as it is in virulence, it is entirely unlikely that in the majority of instances it ever would have been identified as a related form of the tubercle bacillus. At the present time, however, if the situation demands, the procedures are at hand for its transformation into a typical tubercle bacillus of known virulence and type.

A similar situation previously unrecognized, I believe, has recently arisen as the result of the curious acid-fast strains described by Pinner<sup>31</sup> and by Norton<sup>25</sup> who have isolated them from perfectly well authenticated cases of tuberculosis. These organisms are for the most part avirulent, but not invariably so. Although culturally one would not usually suspect them of being acid-fast bacilli, microscopic examination reveals them as indistinguishable in this respect from true tubercle bacilli.

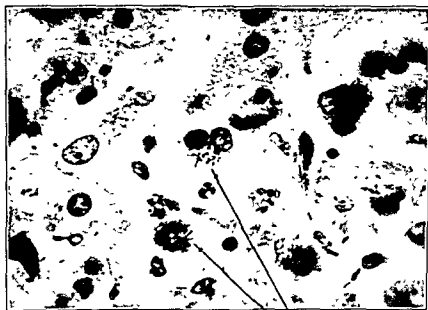
Some of them are fairly luxuriant growers and markedly chromogenic, while others grow much more scantily and the colony structure recalls that of the typical diphtheroid. They are probably closely related forms since the character of pigmentation among microorganisms is a very variable one. The fact that strains practically indistinguishable from this group have been dissociated from the filtrates of one of our bovine strains, offers more than a suggestion that their presence in the human case may be similarly explained.



Although it is out of place to discuss here in too great detail atypical pathological responses as they may reflect the dissociation *in vivo* of anomalous variants of the tubercle bacillus, the point certainly is entitled to brief mention. I have become repeatedly impressed with this point through the years because we have been able to diagnose pathological material as atypical tuberculosis, which textbooks would scarcely condone. It has always been our belief that certain of these atypical, pathological responses might be correlated with dissociation changes of the organism because our previous studies have frequently shown that this has been so with other microorganisms.<sup>10</sup> And there is no *a priori* reason why the tubercle bacillus should be an exception.

In fact, for some years these anomalous responses, particularly with certain strains of the avian bacillus, have been well recognized. The polymorphonuclear response, for example, both within well formed tubercles and in diffuse granulomatous tissue has been repeatedly observed. More recent work of Winn and Petroff<sup>42</sup> enters somewhat more into the detail of the histopathology that can be correlated with different variants of the avian bacillus. Their study indicates that the normal variations in the histopathology of recognized tubercle are to be correlated in part with the varying virulence and biochemistry of the infecting variant.

*Inferences.*—But the inferences from our own evidence carry us into the realm of atypical tubercle, not to say that which on *a priori* grounds might not even be recognized as the lesions of tuberculosis. Merely as one example of this I may refer briefly to tissue response to a new acid-fast variant.



A

Fig. 4.—This section of rabbit liver shows at A the predilection of the acid-fast bacilli for the large endothelial cells of this curious granulomatous process. X 1000.

With this strain the whole reticulo-endothelial system of the liver seemed given over to the production of an endothelioid type of giant cell, multinucleated, apparently for the express purpose of digesting enormous numbers of these acid-fast bacilli. The giant cell is distinctly not of the Langhans' type so characteristic of classical tuberculosis, but resembles much more the epithelioid type found in the lymph glands of Hodgkin's disease, although differing by its remarkable phagocytic proclivities. Viewed broadly the atypical pathological responses may be summarized by saying that the nearer one approaches the saprophytic or nonacid-fast cyclo stages, the more nonspecific becomes the response of the tissues. Now since there are a number of clinical conditions so relatively nonspecific that their tuberculous etiology has been in doubt it may be profitable to review some of them briefly, because of the correlation of their bacteriological findings with the anomalous variants of the organism's life cycle.

*Boeck's Sarcoid.*—In this connection I wish to touch, albeit briefly, on a rather well known condition, Boeck's sarcoid so-called, and the somewhat less familiar condition of benign lymphogranulomatosis, more particularly in its cutaneous manifestations. The latter condition has been made the subject of rather extensive investigations by Schaumann<sup>36</sup> and is characterized by an epithelioid type of granuloma, usually present in the tonsils, the lymphatic glands, the bones and skin. The cutaneous manifestations are rather indistinguishable in many instances from Boeck's sarcoid whose histopathology reposes in that twilight zone between atypical tuberculosis and atypical syphilis. But as the result of his investigations Schaumann believes that his benign lymphogranulomatosis and Boeck's sarcoid are essentially the same thing; which differs somewhat from the original point of view which held that Boeck's sarcoid, although an infectious granuloma, probably had no single etiology. The most common causes attributed to it were the tubercle bacillus and the spirochete of syphilis; but as Schaumann opines, "Boeck's sarcoids are never syphilis for me."

But that the tubercle bacillus may be presumed to exist in these lesions in a low grade or atypical form may be judged first from the fact that in quiescent stages of the disease the tuberculin reaction is almost universally negative; and that cultivation experiments for the organism, as well as animal inoculation, are also negative. Nevertheless, the sputum in these cases when inoculated into animals *serially* may ultimately result in a growth of isolatable tubercle bacilli. And furthermore, from the clinical standpoint such cases are apt, after many years, to develop an active pulmonary tuberculosis with a marked tuberculin reaction.

We have had opportunity to study in detail such a case, which as a matter of fact has been under observation in its quiescent stage for several years and which has recently been made the subject of a clinical report by Crawford.<sup>9</sup> The lymph glands in places were enormously enlarged, but they never showed caseation, although they were riddled with an epithelioid type of tubercle which showed a marked tendency to become fibro-sclerotic. Most striking in this pleomorphic picture were the acid-fast organisms that could be demonstrated in stained sections of the gland; and in this respect they have a striking resem-

blance to the pictures described by Pinner in the lesions produced by his Group III of atypical acid-fast bacilli. Nevertheless, in our case it was quite impossible by any of the conventional methods to isolate these acid-fast organisms or to produce typical tuberculosis in animals. The most that resulted were local abscesses of the type described above. However, serial inoculations were not done.

From the excised gland, however, there were isolated very pleomorphic, diplotheroid bacilli rich in their acid-fast granules; and it now seems to me more likely than ever that this organism represented one of the nonacid-fast cyclo-stages of the acid-fast bacilli. From another of the glands excised from a different location, and at a different time, this bacillus was found in company with a diplococcus resembling in a general way this stage in our experimental cycle of the avian bacillus (Diagram I). Schaumann's position then, that benign lymphogranulomatosis is caused by the tubercle bacillus and probably of the bovine variety, and that Boeck's sarcoid is a cutaneous manifestation of this disease, has much evidence for its support.

*Tuberculous Ultravirus.*—It is interesting to note also that Darier,<sup>5</sup> one of the great authorities on sarcoids, takes the position that the tuberculous ultravirus opens a new and very promising path of investigation into the etiology and pathogenesis of these interesting skin manifestations. He has subjected several such cases to bacteriological study in Calmette's laboratory and the results, although somewhat equivocal are similar in their outcome in guinea-pigs to those resulting from inoculation of sputum and pus filtrates. For some reason serial passage was not resorted to, and one of the animals died of a pseudo-tuberculosis without acid-fast bacilli. Others showed acid-fast bacilli in the tracheo-bronchial glands. He draws attention to the previous defective experimental approach to this problem in the respect that it has failed to make serial inoculations.

He also brings out the point that the cases themselves should be tested with avian tuberculin, and cites such cases which have so responded. It is interesting to recall that our own case reacted to avian tuberculin, although it was quite negative to both the human and bovine varieties. Tuberculides as such had come to be thought of as purely allergic manifestations of tuberculosis, but more recent investigation has indicated their basis in an infarction brought about by acid-fast bacilli present in the small capillaries of the lesions.

*Atypical Lesions.*—There is an increasing tendency to associate certain joint and rheumatic conditions, so-called, with the tubercle bacillus, which is also true to a certain extent with ocular conditions. In fact, the ophthalmologists have furnished rather satisfactory proof that in the eye at any rate atypical lesions of a chronic inflammatory nature may be truly tuberculous, even though giant cells and caseous changes and such classical expressions of the specific lesions be absent. Clinically at least such apparently nonspecific conditions appear as the obvious pacemakers for chronic tuberculosis which ultimately may localize in the lung apices.

## SUMMARY.

It seems pertinent to direct attention to the fact that it is no longer possible to view the tubercle bacillus as an unvarying entity. The evidence is strong that it may go through an evolutionary cycle under the proper environmental conditions.

This cycle is composed of several stages, some of which are so "denatured" that they are no longer recognizable as tubercle bacilli. In fact, they correspond to species usually regarded as distinct from the tubercle bacillus; since some of them are nonacid-fast and capable of multiplying in this form rather indefinitely.

Most, but not all, of these cyclo stages are nonvirulent; but they are potentially virulent in the sense that they are capable of returning to the original virulent stage from which they came. Such transition may become possible by their development at times of gonidial forms, reproductive in nature. Some of these are so small as to pass the pores of clay filters. It seems likely that the classical granules of Much are of this nature.

Partly as a result of this metamorphosis, involving as it does the dissociation of variants of anomalous pathogenicity, the course and clinical manifestations of the disease may be profoundly modified. In fact the clinical types of the disease may sometimes be as anomalous as are the bacteriologic types of the germ associated with them. That a patient may run a low-grade fever, or no fever at all; in short, that he may have all the features of a low-grade sepsis, but without localization is entirely compatible with an epituberculous symptomatology. The attendant diagnostic alertness that its recognition makes possible may at times save the patient needless surgical procedures, if not his life.

On the other hand I would not presume to intimate that anomalous host factors may not play their part at times in the course that the disease may take. Doubtless these variables are interdependent, but it seems desirable to recognize that variability in the parasite is important.

And surgical pathology should by all means have a point of view much more inclusive than that indicated by gross tubercles, caseation, giant cells, etc. It should certainly be able to recognize either epithelioid tubercles or diffuse epithelioid granulation tissue; and even when the latter is not conspicuously epithelioid in character he should suspect an underlying tuberculous background which, in many instances, may eventuate in nothing more than this, if the patient and his physician are properly apprised of the potentialities of the situation. And if the polynuclear responses dominate the exudative reaction, caution should be used about interpreting it as purely pyogenic, or secondary, in the conventional sense of that term.

Both the experimental and diagnostic pathologist should recognize more than ever before that a single inoculation of suspected material into a guinea-pig, by no means rules out conclusively the presence of tuberculosis. Not only this, but that atypical cases may require serial injection of the organ from animal to animal if a greater percentage of positives be demonstrated. Moreover, if the animal happens to be of such unusual susceptibility that it dies with signs of acute sepsis without focal lesions, or with tissue reactions where the polymorphonuclear element dominates, greater caution should be used in adjudging it an irrelevant spontaneous infection, unless positive evidence for the latter be pres-

ent. Careful smear and cultures of the organs and heart blood by newer methods for acid-fast bacilli may be unexpectedly illuminating.

And for the purely research student of tuberculosis the possibility is at least brought into view that certain conditions like Poncet's disease, Boeck's sarcoid, tuberculides, and other conditions perhaps only suspiciously tuberculous may be brought definitely within the widened limits of this condition; and on evidence more substantial than that afforded by the overworked word—Allergy.

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## CHAPTER III.

# ALLERGIC AND IMMUNOLOGICAL CONSIDERATIONS.

K. ROBERT KOCH AND RALPH R. MELLON.

**Reaction.**—When the animal body becomes infected with tuberculosis its reactive power soon becomes altered. First it becomes abnormally susceptible or allergic to tuberculin; and in the second place when the already infected animal is reinfected either no reaction at all, or a very acute reaction takes place at the point of inoculation. This will depend upon whether a small or a large dose is used for superinfection and upon the period elapsed between infection and reinoculation. The acute reaction brought about by larger doses leads first to a nodule, which ulcerates and finally heals. This so-called Koch phenomenon is characterized therefore by two factors: the early appearance of the lesion and the immunity against reinfection.

The early appearance of the lesion means more prompt and extensive damage and death of tissue cells than that seen in the tuberculous infection of the normal animal. The inflammatory response is much more marked in the allergic than the normal animal even when the same number of bacilli are employed; but no qualitative differences are revealed by histologic studies. In explanation of these intensity differences is the fact that tuberculo-protein acts as a much more powerful irritant in the allergic body.

No consensus of opinion exists concerning the interrelationship between allergic inflammation and the establishment of immunity. One opinion assumes a direct and positive relation—a local fixation of the bacilli at the site of entry *by the inflammatory reaction* resulting in the delayed dissemination, as contrasted with the rapid spread in a normal animal body. Willis<sup>10</sup> has shown that lymph nodes draining the sites of cutaneous infection are infectious as early as 24 hours after infection, while the same lymph nodes taken from an immune animal did not become infective before the end of 2 weeks. But such course of events cannot be simply due to a fixation of the bacilli, but must be accompanied also by an interference with growth and actual destruction of the bacilli. Just as in a sensitized body, protein antigens are fixed at the site of injection and produce there intense reactions,<sup>10</sup> derivatives of the tubercle bacillus are possibly fixed at the site of re-injection in the sensitized animal, and thus produce the allergic reaction. However, no experimental data are available to support the contention that such an inflammation will also “fix” the living tubercle bacillus in the sense that its dissemination will be prevented. Klopstock, Pagel and Guggenheim<sup>5</sup> have shown in recent experiments that a nonspecific allergic tissue reaction which closely resembles the tuberculous allergic reaction has no influence upon the spread of the infection. If a very small dose of finely suspended tubercle bacilli is injected either intracutaneously or intravenously into normal and sensitized

animals, as often as not, no allergic inflammation occurs in the tissues of the sensitized animals. But the infection in the normal body leads to a fatal outcome, while the infection in a sensitized body subsides. One may infer that it is not the inflammation as such that protects against infection; but rather its lingering effects on the tissue cells. It is generally agreed that humoral antibodies do not play a rôle in the defense against tuberculous infection.

Concerning tissue immunity, we have no means of a direct experimental proof, yet we are forced to conclude that immune biological forces closely linked to cell function account for the differences in the behavior of normal and sensitized animals. Although no explanation can be given for the development of acquired immunity in tuberculosis, briefly it may be said to be associated with an unknown mechanism which restrains the growth of the bacillus.

All attempts to bring about a refractory state towards tuberculous infection by using either the bacilli killed by heat or by chemicals or their secretion products in cultures have failed. Since living organisms are the only antigens suitable for immunization, the following factors require careful consideration in the evaluation of experimental data.

- (a) Susceptibility of the animal species.
- (b) Virulence of tuberculosis strain and amount of inoculum used for primary infection.
- (c) Period elapsed between infection and reinoculation.
- (d) Amount and virulence of reinoculated strain.

The guinea-pig remains the most suitable animal, because it can be observed in large series best. Yet its high susceptibility to tuberculosis infection does not correspond to the high natural resistance of the human race. Roemer and Hamburger showed independently in extensive experiments the quantitative relations between immunity and reinfection. The effect which the second infection takes, depends especially upon the amount of inoculum used, and to a lesser degree upon the interval between primary infection and reinfection. The immunity is more definite against a small dose than a large dose at any time; and more fully developed against an identical dose at a later period than shortly after the primary infection. Roemer also demonstrated the immunity of tuberculous guinea-pigs against spontaneous infection and the immunity of spontaneously infected guinea-pigs against parenteral reinfection.

The time of observation in experiments carried out on the guinea-pig with virulent strains is restricted by the fact that the primary infection with virulent bacilli always leads to a progressive infection, resulting in the death of the animal within a few months. It is not possible to produce with even a small number of virulent organisms a non-progressive infection which remains stationary for a long time.

Selters<sup>15</sup> experiments, which claimed to have produced a non-progressive tuberculosis by inhalation of small amounts of virulent tubercle bacilli have been severely criticized by B. Lange.<sup>8</sup> Such experiments therefore do not allow any conclusion concerning the immunity condition established in a body in which the tuberculous process was not progressive and healed. In order to reproduce under experimental conditions a chronic non-progressive tuberculous infection,

a species of animal must be selected which has a high natural resistance against tubercle bacilli, or strains of attenuated tubercle bacilli must be used for guinea-pig experiments.

Cattle have been used extensively for such immunity studies, because the human type of tubercle bacilli never leads to a progressive infection in this animal. The question has been raised, whether the results of such an artificial infection could be compared with the immunity established by a chronic infection in the human, because cattle infected with human tuberculosis often do not show any signs of the infection later on; and since, in many of the animals, the signs of the previous tuberculosis inoculation can be detected, the conclusion seems justified, that differences, where they appear, are only quantitative ones.

**Immunity.**—The vaccination experiments on cattle showed that an immunity against artificial infection could be produced which persisted for approximately one year following vaccination. The animals showed greater resistance against reinfection three months following vaccination than 10 to 12 months after Exposure to *natural* contact in infected stables, however, revealed little protection, even if the exposure was limited to not more than one year after vaccination. When the contact was extended over several years, vaccinated and non-vaccinated animals became equally infected. Under natural conditions, the hygienic surroundings in the stables, the feeding and the amount of work to which the animals are subjected, influences their resistance. It has been shown that animals in experimental stables under favorable conditions of ventilation and care showed higher resistance against both natural and artificial infections than animals kept under unfavorable conditions. The limited protection coupled with the danger associated with this method of vaccination involving the excretion of virulent human tubercle bacilli made the method unsuitable as a practical prophylactic procedure.

Immunity studies on guinea-pigs infected with attenuated strains have attracted much attention since Calmette introduced this method for the prophylactic immunization of the human. Krause, Baldwin, Gardner and Willis<sup>6, 16</sup> used in guinea-pig experiments a strain of attenuated virulence. Inoculation of animals, either parenterally or by inhalation, leads to a non-progressive tuberculosis, localized more or less in the glands near the site of entry. The tuberculin sensitivity decreases after 6 to 12 months, but may last up to 2 years. Autopsies of animals failed to reveal any active infection. In agreement with earlier investigators it was shown that tuberculin sensitiveness in reinfected animals reappears within a few days. The protection against reinfection, however, was incomplete, and did not seem less two years following primary infection than after one year. The second infection took in all animals; but the general infection was less in the reinfected animals than in the controls.

B. Lange<sup>9</sup> used in his experiments a bovine strain, which showed an attenuated virulence. When used for intracutaneous inoculation in doses of  $10^6$  to  $10^8$  mg. the infection remained mostly restricted to the site of the injection and the course of disease was benign. Some of the animals still survived after 12 to 15 months observation. Corresponding to the slower development of the tuberculous process after inoculation with the attenuated strain, the protection also



develops more slowly; but even at its height it never reaches the degree obtained by virulent vaccination. In fact, complete immunity could not be established with the attenuated strain against the small dose of  $10^{-7}$  mg. of virulent bacilli tracheally or parenterally introduced. Control animals infected with virulent tubercle bacilli and reinfected at the same time with the same dose revealed complete protection.

Morphological examination of the super-infected animals killed at varying periods after reinfection showed certain characteristic changes. In animals, in which complete protection was attained, the reinoculations failed to produce a focal infection; also the regional lymph glands remained free of disease. On the other hand, when immunity was absent, the reinfected focus developed was analogous to a primary focus, being accompanied by unlimited propagation of the process. According to varying degrees of immunity between absent and complete protection, the extension and intensity of the pathological process varied. Animals were observed in which the focal reinfection resembled the primary focus, yet the extension of the specific disease was limited or the propagation of the super-infection remained restricted to the regional lymph nodes. An inflammatory focus was never observed at the site of reinfection without involvement of the lymph nodes.

*Contrasting Opinions.*—In contrast to the generally accepted conception of the relation of immunity to the presence of tuberculous tissue, Calmette<sup>3</sup> is of the opinion that only the allergic state is dependent upon the presence of tuberculous tissue and that immunity can be established through the mere presence of an avirulent microorganism, a "harmless parasitism." "The immunity exists only as long as the organism harbors a small amount of specific virus and it leads to a resistance, or a more or less distinct intolerance towards new infection by the same specific virus." According to Calmette a culture of tubercle bacilli suitable for immunizing purposes should be devoid of virulence and incapable of giving rise to progressive tuberculosis lesions experimentally. It should also preserve the antigenic properties of virulent tubercle bacilli as well as its capacity of giving rise to tuberculins in artificial culture medium and to antibodies in animals which are free of any virulent infection. As proof for immunity established by avirulent tubercle bacilli, Calmette enumerates the appearance of serological reactions and changes in the blood sedimentation time, following the inoculation with avirulent tubercle bacilli.

The strain employed by Calmette and Guérin, generally known as BCG is supposed to be of such character. The culture of bovine type was originally virulent but lost its virulence through serial inoculations of the cultures on 5 per cent. glycerinated potato ox-bile medium. Calmette believes that he succeeded in this way in modifying hereditarily the physico-chemical constitution of the bacillus by inducing it to grow on an extremely alkaline medium peculiarly rich in lipoids. After thirty successive inoculations on this medium, at intervals of 25 days, the culture became avirulent. Calmette considers a strain avirulent when it does not produce disseminated tuberculosis which is not fatal nor capable of reinoculation.

According to Calmette and the majority of investigators, the strain produces either no tuberculous lesion at all or lesions of purely localized nature, which instead of becoming caseous undergo regressive changes and disappear. Whether ingested or introduced parenterally it is tolerated well. The microbic elements accumulate in the lymphatic organs, grow there for a variable length of time and are eliminated by the normal excretory channels.

Subcutaneous doses up to 1 mg. produce in the guinea-pig a slight local swelling which disappears within two weeks. Doses of 3 to 10 mg. lead to an abscess ulcerating around the tenth day and healing within four to eight weeks leaving behind a slight enlargement of the lymph nodes. Doses of 100 mg. to 1 Gm. produce the same type of local lesion and tuberculous follicles disseminated in various organs, and which disappear. Animals infected with such large doses show a decreased resistance to secondary infection. Intraperitoneal injection of over 3 mg. leads to an infection of the mesentery with tuberculous nodules; but it is not progressive and disappears in three to five months. After intracardial injections of 1 to 10 mg. the only effect seen is a general swelling of the glands, setting in two weeks after inoculation and lasting for ten days. The BCG strain has been found viable in abscesses as long as  $2\frac{1}{2}$  to  $6\frac{1}{2}$  months after inoculation without change of its characteristics. Usually lesions produced by BCG are not transferable to other animals.

Within two to four weeks after BCG inoculation cutaneous tuberculosis allergy may develop; if present, it reaches its maximum between four and eight weeks and may persist as long as 240 days after inoculation. In contrast to Calmette's contention of the independence of allergy and immunity a number of investigators found that in guinea-pigs the cutaneous allergy followed closely the degree of resistance against virulent tuberculosis infection.<sup>2</sup> Intradermally inoculated animals developed a most durable and most intense cutaneous allergy, and such animals showed the greatest resistance; while the least stable allergy, and the least resistance was observed following oral inoculation of BCG. Under the conditions present in these experiments there seems to be little doubt of the association—perhaps the relationship—of allergy and immunity.

The course which the reinfection with the virulent tubercle bacilli takes after the latent period, is identical in vaccinated and non-vaccinated animals when the reinfection is introduced parenterally. The natural course of the infection is simply postponed. The most suitable animal for the demonstration of the efficiency of BCG according to Calmette is the monkey. However, the experience of Wilbert, upon which Calmette relied, has not to our knowledge been confirmed. The inoculation experiments on cattle have not yet led to an agreement among the various authors. There is evidence that in trials of short duration BCG vaccination may retard the development of tuberculosis, but when cattle continue under exposure to natural infection, resistance diminishes and tends to disappear. In most of the experiments reported, observations have been limited to not more than one year. In the investigations of the Canadian National Research Council immunity trials varied up to  $4\frac{1}{2}$  years. They found evidence of tuberculous lesions at autopsy in 78.4 per cent. of vaccinated animals and in 75 per cent. of unvaccinated cattle.

Calmette originally recommended oral administration of BCG, basing his conception upon the Besredka theory, that a local immunization should be established in those tissues which in infants are the port of entry for the micro-organism, namely, the intestinal tract. The anatomical findings of Disse demonstrated that the epithelium of the intestines is formed only around the ninth day of life. Up to then the mucosa of the intestines consists of a syncytium, which permits invasion by the organisms. However, it has been shown that after oral administration of BCG, tuberculin sensitiveness is established only in a small percentage of animals, and the latent period after reinfection is shorter and more irregular than the one obtained by parental administration of BCG.

*Experiments.*—All experiments in which the production of progressive tuberculosis after experimental infection with BCG has been reported may be divided into two groups:

1. The development of infection was the result of special susceptibility of the infected animal or animal organ, (cornea, brain), not the result of increased virulence. The incidence of such infections is very low when large series are observed. The general physical condition of the animal in which lesions are found, is not influenced by factors pertaining to food or environment. Attempts to establish progressive tuberculous infections by reinfection of normal animals usually fail.

2. Cultural dissociation of the BCG strain into the virulent and avirulent variants was first demonstrated by Petroff<sup>11</sup> and confirmed by Begbie,<sup>1</sup> Seiffert<sup>14</sup> and Christianson.<sup>4</sup> (Somewhat fuller discussion of this and related points is given in the section on variation and life cycles.)

It is pertinent that a particular type of variant dissociated from one culture may be virulent, while a similar form dissociated from the same culture at another time may be completely lacking in virulence. This must be kept in mind when the pros and cons of certain results are being debated. The S type dissociated from BCG does not grow on bile glycerol potato media. It does not seem to be very resistant to changes in the environment, and it is pathogenic. While Petroff found it only pathogenic for guinea-pigs, Seiffert's forms were also virulent for rabbits. The R variant is the type of colony of which the Calmette strain is composed when grown on ox-bile glycerol potato. Dissociation can be accomplished only on bile-free media and is a rare occurrence even after repeated sub-cultures.

The important practical point would be to determine whether the tissues of the human body are a suitable medium for the dissociation of the virulent type from the non-virulent; and if so, does their virulence continue to increase. The majority of evidence available so far rather indicates that this is not the case at the moment. Some emphasize the necessity of an adequate consideration of the time factor. The fact that even virulent bovine bacilli tend to localize and disappear in the human body, as the child's age increases, may indicate that attenuated bovine bacilli would tend to do so even to a greater degree. In a final analysis, carefully controlled clinical observations on large numbers of vaccinated children will give the answer. Animal experiments have not afforded categorical evidence for the efficiency of the method as an immunizing procedure.

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## CHAPTER IV.

# THE PATHOLOGY OF PULMONARY TUBERCULOSIS.

RICHARD H. JAFFÉ.

### INTRODUCTION.

**The Histopathology of Tuberculosis.**—When tubercle bacilli gain entrance into a suitable host they produce alterative, exudative and proliferative changes the extent and intensity of which depend upon the resistance of the host and upon the number and virulence of the bacilli.

The *alterative changes* culminate in necrosis which may affect either the preëxistent normal structures (primary tissue necrosis) or the products of the exudative and proliferative processes. These different forms of necrosis usually pass into each other. Some investigators, therefore, deny the primary tissue necrosis or attribute little significance to it, stressing that the tuberculous inflammation starts with exudation and proliferation, respectively. In cases of overwhelming infection or complete lack of resistance (anergy) the primary tissue necrosis, however, dominates the anatomical picture while exudation and proliferation are insignificant or completely absent. With increasing resistance the exudative and proliferative response to the infection becomes more and more marked and the primary damage done to the tissue by the invading microorganisms escapes detection.

The *tuberculous exudate* consists of the fluid constituents of the blood which escape from the irritated and abnormally permeable blood-vessels and of cells which, too, are chiefly derived from the blood stream. The fluid part of the exudate may not change its physical properties after leaving the blood-vessels or it may coagulate or fibrin may segregate from it. It is most abundant in places where space permits it to accumulate as in the serous cavities of the body, in the subarachnoidal spaces of the leptomeninges or in the air spaces of the lung. The tuberculous exudate contains different forms of cells. Experimental studies have shown that the first cells to appear at the point of infection are polymorphonuclear leukocytes. A few hours after tubercle bacilli have been injected into the lung or into loose connective tissue they are found surrounded by leukocytes which take them up but soon succumb to their toxic action. A few erythrocytes, too, are usually present. With the beginning of the disintegration of the leukocytes the cellular picture of the exudate changes. Mononuclear elements now are found to be predominating. They are the monocytes and lymphocytes of the blood and are joined by the mobilized free and fixed wandering cells (clasmatocytes, histocytes) of the adjacent tissue. The bactericidal action of the mononuclear cells (macrophages) is superior to that of the leukocytes (microphages). The macrophages display active phagocytosis which is directed against the bacteria as well as against the degenerating leukocytes

The fate of the tuberculous exudate varies. If natural or acquired resistance is high the exudate may become resorbed without undergoing further changes and normal conditions may be restored. This is the most favorable outcome of the tuberculous infection which is seen especially in the "transient tuberculous infiltrations" of the lung. Greater susceptibility to the tuberculous toxins leads to necrosis and caseation of the exudate. The term "caseation" was introduced by Virchow who compared the products of tuberculous necrosis with reindeer's cheese. This comparison is not purely morphological since, like real cheese, the caseated tuberculous material consists of coagulated proteins and finely dispersed fat (H. G. Wells).

The caseated tuberculous exudate may become inspissated by resorption of its watery content. It now resembles old Dutch cheese. About the dry and firm material a capsule of dense connective tissue is formed or the entire cheesy area becomes substituted by scar tissue that develops from islands of connective tissue inside the caseated focus which have escaped destruction. A frequent late result of caseation is calcification. Lime salts from the tissue fluids crystalize about the debris of the broken down structures and in the early stages these lime salts often arrange themselves in the form of concentric rings similar to the Liesegang rings which play an important rôle in colloidal chemistry. Under certain conditions calcification may be followed by ossification.

While encapsulation, fibrous replacement, calcification and ossification are successful attempts of the body to localize the tuberculous infection and can be considered as morphological signs of a high resistance acquired during the course of the infection, the changes to be discussed next are unfavorable since they lead to spreading of the infection. These changes consist of softening and liquefaction of the cheesy material. The softening is due to an absorption of water, to a swelling of the necrotic cellular debris, a physical phenomenon which can be compared with the swelling of gelatine (Huebschmann<sup>1</sup>). The liquefaction which indicates great susceptibility to the tuberculous toxins is the result of an immigration of polymorphonuclear leukocytes which, by breaking down, liberate proteolytic enzymes. These enzymes digest the caseated material. Large areas of caseation may first become sequestered and a clump of cheesy material then is seen floating in pus until it, too, melts down.

*Proliferative Changes.*—The proliferative changes follow the exudation immediately. They start with the appearance of the mononuclear cells since these cells undoubtedly take part in building up the tuberculous granulation tissue.\* In case of favorable response to the infection the proliferative changes may start so early that the exudative stage of the infection is more or less obscured. Under the specific action of the tubercle bacilli or their metabolic products the mononuclear cells of the exudate swell up and develop into large, pale stained cells with vesicular nuclei. Because of the resemblance of these cells to epithelial cells Virchow called them "epithelioid cells," a name which has

\*Long points out that, in general, the protein fraction of the tubercle bacilli is responsible for the acute exudative phenomena while the lipoids are concerned in the more chronic exudative and productive manifestations (see especially Sabin and her co-workers). The carbohydrates play a part in the serological and antibody reactions

caused much confusion but is still generally used. The name "tubercle cells" or "tuberculoocytes" suggested by some investigators is not very appropriate since these cells are not restricted to the tuberculous infections but are also found in other types of inflammatory granulation tissue. By amitosis the nuclei of the epithelioid cells may divide. The nuclear division is not followed by cellular division and multinucleated cell forms result in which the nuclei soon accumulate near the periphery. The nuclei now shrink and stain deeply. These are the "Langhans giant cells." The question whether there are different forms of giant cells in the tuberculous granulation tissue is more of academic than practical interest.

In addition to the mononuclear cells of the exudate the mesenchyme about the initial tuberculous lesion takes an active part in producing the epithelioid cells. In the later stages of the inflammation it supplies the bulk of these cells. About the histogenesis of the epithelioid cells from the fixed tissue cells much has been written and since the earliest descriptions to the present day, the opinions of the different investigators have been divided. In this connection it is sufficient to state that the majority of the epithelioid cells are derived from the active mesenchymatous cells which are scattered between the fibrocytes, are most numerous about the blood-vessels and belong to the reticulo-endothelial system.

*The Tubercle.*—The epithelioid cells form nodules the shape of which depends upon the mechanical conditions of the location. If the resistance to spreading is the same in each direction the nodules are more or less spherical. Differences in the resistance lead to oval, flat or irregular nodules. The tubercle grows by apposition of new epithelioid cells in the periphery or by fusion of adjacent nodules. Around the epithelioid cell tubercle there is usually a zone of nonspecific cellular infiltration composed of lymphocytes, plasma cells and fibrocytes. This zone occasionally contains also neutrophilic and oxyphilic leukocytes.

The typical epithelioid cell tubercle centers about a caseous area which is the remnant of the initial caseated exudation. It is only in certain very benign forms of productive tuberculosis, especially of the lymph nodes and the spleen, that the tubercle starts as such or that the preliminary exudative changes are completely obscured. From the caseated center the regressive changes may spread to the newly formed granulation tissue beginning with fatty degeneration and terminating into caseation. With the caseated exudate the caseated granulation tissue forms a uniform mass the ultimate fate of which is similar to that of the purely exudative caseation, namely encapsulation, fibrous replacement or calcification or softening and liquefaction.

In the older literature the caseation of the tubercle has often been explained as the result of lack of nutrition since it was believed that tubercles contained no blood-vessels. This explanation, however, is not correct because fine capillaries extend between the epithelioid cells though they are less conspicuous than in other forms of productive inflammation. In addition, even very large and compact epithelioid cell tubercles may escape caseation. Hence, there is no doubt that caseation of the tubercles is due to the same cause as the primary tissue necrosis and the caseation of the exudate, namely, to the toxic action of the bacilli.

In the walling off of the central caseated area by scar tissue the epitheloid cells play an important rôle. These cells are not only able to phagocytize the tubercle bacilli but they produce also collagenous ground substance. In young tubercles a fine reticulum can be demonstrated between the epitheloid cells. Part of this reticulum may be the remnant of the preëxistent reticulum of the affected organ but it is too abundant to be merely preformed. Most authors, therefore, assume that the greater part of the reticulum is a product of the epitheloid cells. The reticulum later becomes replaced by fibrillar connective tissue while the epitheloid cells shrink. The connective tissue of epitheloid cell origin has the tendency to undergo hyalinization. Thus, the caseous or calcified center becomes surrounded by a dense hyaline scar. Some of the scar tissue is also formed by the nonspecific productive changes in the periphery of the tubercle. This later connective tissue retains its fibrillar structure much longer than that produced by the epitheloid cells.

Krause and others have tried to link the morphology of the defense reactions with the allergic state of the infected individuals and consider the tubercle as characteristic of the normergic response while the acute, exudative inflammation is supposed to be the essence of the allergic reaction. This conception does not agree with the observations made especially in human tuberculosis. Thus, the first stage of the pulmonary primary lesion is exudative in character. Generally speaking, there is nothing specific about the allergic inflammation. No elements are introduced into it which are not also present in the normergic inflammation. The differences are merely qualitative, the allergic inflammation being characterized by the quicker appearance and greater intensity of the changes. This holds particularly true of tuberculosis (Rich).

*Perifocal Reactions*—The discussion of the histopathology of the tuberculous changes would not be complete without considering the so-called "perifocal reactions." The perifocal reactions are exudative and indicate a great susceptibility of the tissues to the tuberculous toxins. Because of the abnormal permeability of the cells which are in a state of high irritability the toxins diffuse freely from the focus of infection into the surrounding tissue. As they permeate the tissue the toxins become more and more diluted (Tendeloo<sup>2</sup>). The exudate is hemorrhagic, fibrinous or serous, contains a varying number of polymorphonuclear leukocytes and mononuclear cells and is capable of quick resorption when the resistance increases and the permeability diminishes. Although a marked perifocal reaction may lead to extensive exudation and, for instance in the lung, may produce a massive, sudden infiltration, it exerts also a favorable effect since it causes a dilution of the toxins and stops their diffusion by blocking the lymphatics.

### HISTOPATHOLOGY OF PULMONARY TUBERCULOSIS.

Before describing the special histological features of pulmonary tuberculosis a brief discussion of the normal micro-anatomy of the lung is necessary since the modern concept of pulmonary tuberculosis is based upon it. The anatomical unit of the lung is the "acinus" (Loeschcke,<sup>3</sup> Nicol,<sup>4</sup> Husten<sup>5</sup>, Aschoff<sup>6</sup>). As the unit of a lobular gland is arranged about a small excretory duct, thus, the



pulmonary acinus is arranged about a terminal bronchiolus. The terminal bronchiolus which is lined by ciliated epithelium and possesses a well developed muscular and elastic wall breaks up under a right angle into two respiratory bronchioli of the first order which carry the first alveoli (see Fig. 1). The respiratory bronchioli of the first order divide dichotomically into those of the second and third order respectively which too, have alveolar outpouchings of their wall located opposite the accompanying artery. From the respiratory

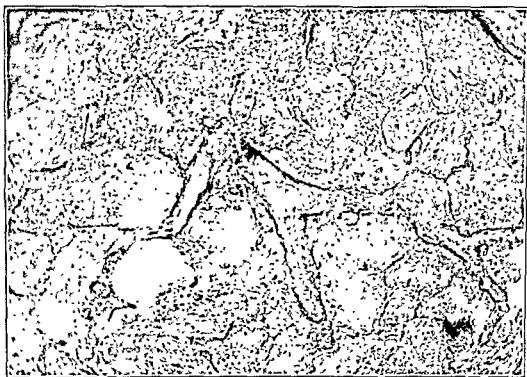


Fig. 1.—Focal caseous pneumonia (see also Figs. 13 and 14). The picture shows a small bronchus dividing into two terminal bronchioli. The upper terminal bronchiolus is seen dividing into two bronchioli respiratorii of the first order, the lower of which breaks up into two bronchioli respiratorii of the second order. Note the alveoli originating from the wall of the bronchiolus respiratorius of the first order. Weigert's elastin stain. X 150.

bronchioli of the third order up to five alveolar ductuli branch off. The alveolar ductuli contain alveoli on all sides which are separated by circular muscle fibers. According to W. Snow Miller<sup>7</sup> these muscle fibers form a sphincter at the distal end of the alveolar ductuli. The alveolar ductuli terminate into the alveolar sacs.

The most important mode of infection of the lung with tubercle bacilli is by way of the air route. It has been suggested that the inhaled or aspirated bacilli become lodged first in the narrowest part of the bronchial tree which is the part above the point of division of the terminal bronchiolus into the first respiratory bronchioli and that from here the inflammation extends into the acinus. Experimental investigations and studies on early human pulmonary lesions

indicate, however, that in the majority of instances the tubercle bacilli reach the alveoli directly and that it is in this location that the first reactions take place.

The earliest stages of pulmonary tuberculosis are known from animal experiments only. In the lung the initial alterative changes are apparently very insignificant and exudation is first to become *microscopically visible*. But there are cases of very severe infection of the lung, especially in young infants, in which the primary tissue necrosis is very pronounced (Huebschmann<sup>1</sup> and others).

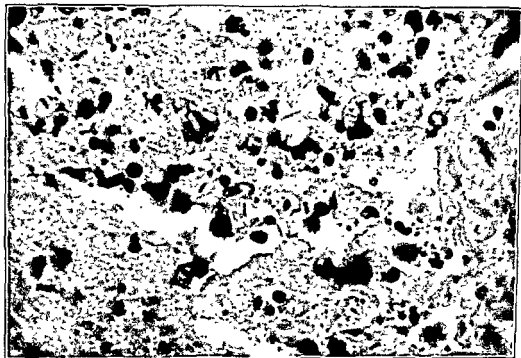


Fig. 2—Early tuberculous exudate in a pulmonary alveolus. Note the slender tubercle bacilli between the degenerating pus cells and small round cells Ziehl-Neelsen stain with carbolfuchsin, X 1200

*Exudation.*—The exudate accumulates chiefly in the air spaces. It is serous or sero-fibrinous in character. At first polymorphonuclear leukocytes and small round cells of hematogenous origin predominate (Fig. 2). Later, they are outnumbered by large round or oval cells with an ample, finely vacuolated cytoplasm and vesicular or bean shaped nuclei. The cytoplasm contains small lipid droplets and often also phagocytosed inclusions of cellular remnants. In gelatinous pneumonia the alveoli are stuffed with these cells which have been designated as "alveolar phagocytes." The origin of the alveolar phagocytes is still under discussion. Those authors who maintain that the pulmonary alveoli possess an incomplete epithelial lining consider the alveolar phagocytes as swollen, proliferated and desquamated epithelial cells while those investigators who deny the presence of epithelial cells in the alveoli trace the phagocytes to the mesenchymatous elements in the alveolar walls or to emigrated nongranu-

lated cells of the blood. My own studies have convinced me that the alveolar phagocytes of human beings originate around the alveolar capillaries and that, by passing into the alveolar spaces, they often arrange themselves in an epithelial-like fashion (Fig. 3).

*Caseation of Exudate.*—When the tuberculous exudate is not resorbed it undergoes caseation and the caseation quickly spreads to the wall of the alveoli (Fig. 4). It is an interesting and important fact that the elastic structures are very resistant to the caseation and that they persist almost indefinitely though all

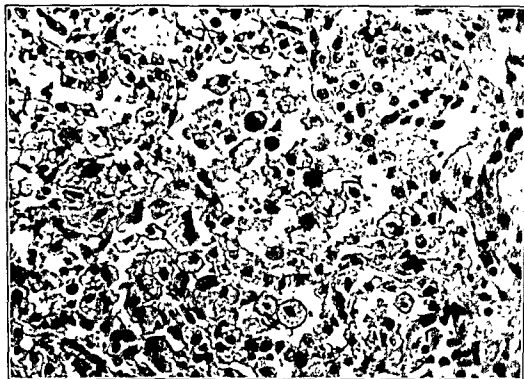


Fig. 3.—Alveolar phagocytes in an early tuberculous pneumonia. The alveoli are filled by large mononuclear cells with vacuolated cytoplasm. The origin of these cells from the alveolar septa is very distinct. X 600.

the other tissues are completely destroyed (Fig. 1). In encapsulated caseous foci of many months' and years' duration stains for elastin still reveal the outlines of the alveoli, bronchioli and blood-vessels.

Exudative reaction into the alveolar spaces also occurs when the tubercle bacilli are brought to the lung by the blood or lymph-stream or invade the lung by direct extension from adjacent organs. In the case of hematogenous infection of the lung the tubercle bacilli are excreted into the alveoli, either free or enclosed in macrophages.

*Tubercle Formation.*—Concerning the productive tuberculous changes in the lung there are two possible sources for the epithelioid cells and giant cells, namely the mesenchyme in the alveolar septa and about the blood-vessels and bronchi, and the cells of the alveolar exudate. The majority of the tubercles develop from

the histocytic elements about the alveolar capillaries (Fig. 5). The tubercles bulge into the alveolar spaces and lead finally to their obliteration. Some of the tubercles originate also in the lumen of the alveoli, the alveolar phagocytes assuming the appearance of epithelioid cells and giant cells and arranging themselves to nodules. W. Snow Miller<sup>8</sup> has shown that a certain form of tuberculous pneumonic exudate is characterized by the intraalveolar production of a reticulum which is connected with the thickened reticulum of the alveolar walls.



Fig. 4.—Exudative miliary tubercle of the lung In the center of the picture is a focal area of caseous pneumonia which is surrounded by a perifocal zone of serous exudation. The section is taken from a case of early generalization X 150.

While the elastic tissue of the lung resists exudative caseation it is destroyed by the productive processes. When tubercles are formed the elastic fibers disappear and in caseated tubercles elastica stains fail to disclose the framework of the lung.

Whether the pulmonary changes are exudative or productive they spread along the acini (acinous dissemination). The characteristic clover leaf or garland-like arrangement of young tuberculous lesions about fine bronchioli is due to this acinous dissemination. When the aspirated bacilli-containing material infects the area which is supplied by a terminal bronchiolus the tuberculous focus corresponds to the whole acinus. Isolated infection of respiratory bronchioli or alveolar ductuli results in subacinous lesions [acinous tuber-

culosis (Aschoff) ]. By confluence of the acinous and subacinous lesions larger conglomerate foci are formed [acinous-nodose tuberculosis (Aschoff) ].

In recent years the histological studies of pulmonary tuberculosis have been dominated by the attempts to correlate the anatomical manifestations of the disease with the allergic state and resistance of the body. Primary tissue necrosis and rapidly cascating exudation with extensive perifocal reaction, liquefaction and suppuration are considered as the morphological expressions of a high



Fig. 5—Young epithelioid cell tubercles (interstitial form) in a case of acinous tuberculosis of the lung. X 300

susceptibility to the tuberculous toxins. Productive inflammation and induration suggest high resistance. Elastica stains allow the differentiation of the various types of tuberculous lesions even after they have become completely encapsulated. The careful histological examination of a lung with progressive tuberculosis reveals that the different forms of response are not fixed but that there are constant fluctuation periods of great susceptibility alternating with periods of increased resistance. Thus, we may find in a lung large areas of confluent caseous bronchopneumonia with extensive and recent cavity formation showing the complete terminal breaking down of the resistance. Other portions of the lung contain old cavities with dense sclerotic walls, and inspissated caseous foci surrounded by anthracotic scar tissue. In sections stained for elastic fibers some of the caseated fibrotic lesions prove to be the remnants of previous exudative attacks while others have been called in existence by

productive processes. Crops of recent acinous or acinous-nodose tubercles complete the picture. The spreading in progressing pulmonary tuberculosis is not only by aspiration from liquefied older lesions. No doubt, tubercle bacilli often enter the blood stream and are carried back to the lung to be excreted into the alveoli. Acinous lesions may grow by direct extension into adjacent acini and also the lymph stream helps to convey the bacilli to other portions of the lung. Taking all these possibilities into consideration the tremendous complexity of the anatomical and histological picture of pulmonary tuberculosis becomes apparent and one can justly say that no two cases look alike though superficial examination suggests a great monotony of the changes.

### DIFFERENT FORMS OF PULMONARY TUBERCULOSIS.

**Three Stages.**—In analogy to syphilis K. E. Ranke<sup>9</sup> distinguished three stages in the course of the tuberculous infection which he based upon the types of organic lesions and upon the allergic state and resistance of the infected organism. Ranke's publications have caused much discussion in the tuberculosis literature and though some of his statements are open to criticism\* his classification forms a valuable basis for further investigation. As the primary stage Ranke designates the period which immediately follows the first contact of the host with the tubercle bacilli and which includes the changes at the point of entrance of the bacilli as well as those in the tributary lymph nodes. This *first stage*, the stage of the primary complex, is so well established that it has been generally accepted. The *second stage* develops from the first stage by a diffuse dissemination of the bacilli. It is the stage of generalization. High susceptibility opens to the bacilli all possible ways of distribution among which the blood stream is the most important one. By overcoming the barrier of the lymph nodes the tubercle bacilli gain entrance into the blood which carries them to the different organs. Because of the high toxin production there is an intensive attack upon the tissue which is met by a strong perifocal reaction which is characteristic of this stage. We find here the first objection to Ranke's classification. Has really every case of progressive tuberculosis in later life to pass through this second stage? If so the generalization must be usually very mild since it escapes clinical detection. The *third stage* is that of the isolated tuberculosis of a single organ or organ system as for instance the lungs or the urinary tract. It is marked by a relatively high resistance which confines the infection to one organ and influences its course in this organ. It is, however, questionable whether every case of tuberculosis of the lungs develops from a hematogenous focus in the lung which has been left over from the period of generalization and which has remained dormant, often for many years, until for some unknown or suggested reason it starts to progress. Much evidence speaks in favor of the possibility that a considerable number of cases of isolated pulmonary tuberculosis are the result of a new

\*In his masterly discussion of the rôle of allergy and immunity in the pathogenesis of human tuberculosis A. R. Rich devotes but one chapter to Ranke's work which, I think, does not do full justice to this fundamental contribution.

infection, of a superinfection engrafted upon the old primary complex contracted in early life. In addition to the isolated progressive tuberculosis of a single organ there occurs also, long after the primary stage has passed, generalizing forms of tuberculosis in which the involvement of the lung is associated with a tuberculosis of other organs. We can distinguish, therefore, between an early and a late generalization.

In spite of these objections Ranke's work is one of the most valuable recent contributions to our knowledge of tuberculosis and is perhaps the best starting point for a discussion of the pathology of pulmonary tuberculosis.

## THE TUBERCULOUS PRIMARY LESION OF THE LUNG.

### (I. The Primary Complex of Ranke.)

*Definition.*—According to Ranke, the tuberculous primary complex is the result of the first contact of a virgin organism with the tubercle bacilli and represents, therefore, the normergic reaction to the tuberculous infection. It consists of a lesion at the port of entrance of the bacilli (the primary lesion) and of a specific satellite lymph-adenitis which usually surpasses in extent and intensity the changes at the port of entrance. The lymph nodes are the mirror of the region from which they drain (the law of Parrot). Neither the changes at the port of entrance nor those in the regional lymph nodes are typical of the first stage of the infection but it is their constant association which is characteristic of the primary complex and which occurs but once in life save for the very rare cases in which the result of the first infection has been completely eliminated and virgin conditions have been restored.

*Frequency of the Tuberculous Primary Lesion of the Lung.*—If special care is taken in examining the lungs from 70 to 80 per cent. of the autopsies reveal a pulmonary primary lesion. The incidence, however, is perhaps even higher than these figures indicate since it is very likely that, in the course of years, a primary lesion of the lung may become completely obscured. The percentages given for the extrapulmonary primary lesions vary greatly and especially with regard to the intestinal location great discrepancies can be noted among the different authors. Some investigators speak of 3, others of 4, 10, 12 and 16 per cent. (Ghon, Siegmund, Beitzke, Huebschmann, Kudlich and others) and M. Lange even reports 26.8 per cent. In general, I am inclined to consider 10 per cent. as the upper limit.\* While in the majority of the cases the pulmonary primary lesion remains well characterized for the rest of the life the intestinal primary lesion which is a small ulcer heals quickly and one has to rely, therefore, entirely upon the changes in the mesenteric lymph nodes which, in the advanced stage of calcification, are of limited significance. Calcification of the mesenteric lymph nodes may not only be due to

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\*In a recent, very careful anatomical and bacteriological study Blacklock (Glasgow) found among 283 cases of tuberculosis in children below 13 years of age, 101 (35.7 per cent.) which strongly suggested a primary intestinal infection. In his material the high incidence of infections with the bovine strain of tubercle bacilli is striking (32.7 per cent.). (Blacklock, J. W. S. Tuberculous Disease in Children: Its Pathology and Bacteriology. Medical Research Council, Special Report Series No. 172. London. Published by His Majesty Stationary Office, 1932.).

causes other than tuberculosis as for instance typhoid fever, nonspecific suppurative lymphadenitis or parasites, but it may also be secondary to a tuberculosis of the thoracic lymph nodes. In other locations tuberculous primary lesions are very rare. I mention the skin (ritual circumcision!), the vulva, the labia majora, the tonsils, the middle ear, the Eustachian tube and the conjunctiva. Contrary to Baumgarten's conception of the great importance of the trans-placental infection of the fetus, congenital tuberculosis is very rare and the literature contains only a few cases which stand a rigid critique.

**Time of Contraction of the Tuberculous Primary Lesion of the Lung.**—Judging from the recent lesions the first infection may occur soon after birth. Tuberculous primary lesions have been found in the lungs of infants which were but a few weeks old. Huebschmann<sup>1</sup> states that about 60 per cent. of the recent pulmonary primary lesions are found in children below the age of 15 years, that the frequency is highest in children between 2 and 3 years of age and that after the age of 10 years the incidence drops sharply.\* After puberty and especially in advanced age recent primary lesions are very rare (Kalbfleisch,<sup>10</sup> Ragnotti<sup>11</sup> and others). The age does not influence the picture of the primary lesion

**Number and Location of the Tuberculous Primary Lesion of the Lung.**—According to Ghon<sup>12</sup> 83.53 per cent. of the cases show a single primary lesion of the lung and 8.83 per cent. show two such lesions. In the remaining cases up to 5 lesions were counted (see also Kuess,<sup>13</sup> Lange,<sup>14</sup> Pagel<sup>15</sup> *et al*) The fact that even in the case of a known continuous exposure of small children a single primary lesion is the rule indicates that the allergy which prevents the further take of the infection develops very quickly. It seems to me, however, that under the whip of often repeated superinfections the primary lesions progress much more rapidly and also spread much faster along the draining lymph passages than in the cases in which there is no interference with the local defense reactions by the frequent inhalation of tubercle bacilli.

The tuberculous primary lesion selects the parts of the lung which have the best respiratory ventilation, namely the middle fields. The lower half of the upper lobes and the upper half of the lower lobes are the points of predilection (Kuess,<sup>13</sup> Ghon,<sup>12</sup> M. Lange,<sup>14</sup> Blumenberg,<sup>16</sup> Schuermann,<sup>17</sup> Kutsukake,<sup>18</sup> Pagel,<sup>15</sup> Kalbfleisch,<sup>19</sup> Naeslund,<sup>20</sup> Wiese,<sup>21</sup> Farrel<sup>22</sup> and others). The apex of the upper lobe is seldom affected. Of the 166 primary lesions which Ghon collected, 88 were in the right lung and 78 were in the left lung and other authors, too, stress the greater frequency of the primary lesion in the right lung which is apparently due to the greater volume of this lung (Huebschmann<sup>1</sup>).

The pulmonary primary lesion is usually located in the periphery, from  $\frac{1}{2}$  to 2 mm. underneath the pleura. In a few instances it is found in the deeper parts of the lung or near the hilus. The anterior aspect is more often in-

\* Autopsy observations in Buffalo induced Terplan to believe that the pulmonary primary lesions increased in frequency after the second decade of life (Am. Rev. Tuberc., 29: 77, 1934)



volved than the other surfaces. In the bronchi primary lesions are very rare (Ghon,<sup>12</sup> Schuermann<sup>17</sup>).

**Morphology of the Tuberculous Primary Lesion of the Lung.**—The youngest stage of the pulmonary primary lesion is a small focal area of bronchopneumonia, but a few millimeters in diameter. The histological picture is not characteristic. The alveoli are filled by an exudate which is composed of fibrin, leukocytes, lymphocytes and alveolar phagocytes. The alveolar septa



Fig. 6.—Ossification of a tuberculous primary lesion of the lung. On the right side of the picture one sees the remnant of the calcified central area. The mid portion of the picture is occupied by fatty marrow with small round cells and macrophages containing coal pigment. On the inner aspect of the marrow there is a thin layer of bone, while on the outer aspect, bordering at the capsule, there is a thick trabecula of bone. X 150

are thickened and infiltrated by large mononuclear cells. The specific nature of the lesion can be recognized by the presence of numerous tubercle bacilli. About this miliary initial bronchopneumonia there is a zone in which the alveoli are free from bacilli and contain red and white blood cells. In the center of the focus necrosis sets in. The nuclei of the exudation cells break down and the alveolar walls become indistinct. The necrosis spreads quickly to the periphery and in the great majority of the cases the recent tuberculous primary lesion presents itself as an area of caseous pneumonia which is wedge-shaped with a terminal bronchiolus entering the apex of the wedge.

About the caseous bronchopneumonia as center a wall of specific tuberculous granulation tissue is formed which appears first at the side which faces the hilus. This granulation tissue consists of typical epithelioid cells and giant

cells. Together with ingrowing fibrocytes the epithelioid cells produce collagenous ground substance which soon becomes hyaline. The caseous center now is surrounded by a dense specific capsule on the outside of which there is often a thin nonspecific capsule of loose connective tissue with accumulations of small round cells (Aschoff). With the formation of the capsule the primary lesion becomes more or less spherical.



Fig 7—Large wedge-shaped caseous pneumonic primary lesion of the right lower pulmonary lobe with diffuse caseation of the regional lymph nodes. Miliary dissemination in the upper and lower lobe. Colored female child, aged 6 months.

As a rule the pleura over the primary lesion takes part in the inflammation. There is a focal fibrinous pleuritis which has the character of a perifocal reaction. Intensive perifocal reaction may cause massive pleural effusion. When the exudation on the pleural surface is only slight it leads to a circumscribed hyaline thickening of the pleura which is a valuable aid in the search for the primary lesion. When the exudation is more extensive adhesions result.

The fibrocaseous primary lesion may persist as such for many years. In the majority of cases lime salts are deposited in the caseous center and on the inside of the specific capsule and the lesion becomes mortar-like, later chalky

and finally stony in consistency. This calcification may set in very early and may develop within 6 to 9 months. Calcified primary lesions have been found already in infants (Geipel,<sup>23</sup> Kuess<sup>13</sup> and others). With the calcification the involution is not completed. In later life, a young granulation tissue develops from the specific capsule which erodes and penetrates the stony center in form of tongue like projections. Bathed in tissue fluids saturated with the lime salts



Fig. 8.—Tuberculous primary complex of the right lower pulmonary lobe.  
Colored female child, aged 6 months.

the granulation tissue assumes bone forming properties and the calcified center becomes gradually replaced by trabeculae of bone with a fatty or lymphoid bone marrow (Fig. 6). Small calcified centers may become completely substituted by scar tissue and when the adjacent lung tissue becomes emphysematous it may obscure the small fibrosed area which is left.

The process of *encapsulation* and *healing* however, may be interrupted. Acute exudative attacks flare up about the primary lesion which, because of the now higher resistance, do not lead to caseation but are transient and dis-

appear quickly. These are the so-called "primary infiltrations." The breaking of crops of young tubercles through the capsule may delay healing. Young epithelioid cell tubercles appear occasionally also outside the capsule. This interference with the healing causes irregularities in the capsule which becomes very thick or consists of several concentric layers; or about the primary lesion there is much indurated anthracotic scar tissue with bundles of smooth muscle fibers.

The size of the pulmonary primary lesion depends upon the stage of evolution. The recent lesions are from a few millimeters to 2 cm. in diameter but also larger lesions are relatively common (Ghon) (Figs. 7 and 8). The encapsulated calcified or petrified primary lesion of later life has the size of a cherry stone or pea.

With the formation of the specific capsule the pulmonary primary lesion becomes localized and aspiration to other portions of the lung is uncommon because the perifocal inflammation soon obliterates the supplying bronchiolus. Under certain conditions, however, encapsulation does not take place or is insufficient and, by contiguity or aspiration, the primary lesion spreads to the adjacent lung tissue until the entire lobe may become involved. The primary lesion assumes the appearance of a caseous lobar pneumonia (Fig. 9). With the progression of the primary lesion liquefaction and cavity formation (primary cavity, Type I *a*, Schmincke<sup>24</sup>) are often associated. These primary cavities possess an ill defined wall and border at shaggy necrotic lung tissue. Similar to the cavities which form in the later stages of the tuberculosis they may break into the pleural cavity causing a pneumo-pyo-thorax or a pyo-thorax. Massive aspiration with rapidly progressing generalizing tuberculosis of the lungs in form of sublobular, lobular and lobar caseous pneumonias and multiple secondary cavities is another serious complication of the primary cavitation. The main difference from the progressing pulmonary tuberculosis of the third stage is the sparing of the apical portions of the lung.

Cavitation of the primary lesion may also take place after the capsule has been formed (primary cavity, Type I *b*, Schmincke<sup>24</sup>). This cavity has a well defined wall of caseating specific granulation tissue and is usually smaller than the cavity of the type I *a*. But it too may cause dissemination by aspiration. Finally a calcified primary lesion may become sequestered by nonspecific perifocal changes and may be expectorated as a stony concretion (Page<sup>15</sup>).

The serious forms of the pulmonary primary lesion occur when the body is unable to develop sufficient resistance in order to localize the infection. They are found especially in infants and small children, particularly when continuous superinfection stimulates the exudative caseating inflammation to rapid progression, giving the body no chance to build up a wall of defense. Temporary lowering of the resistance by intercurrent diseases (measles, whooping cough and others) or nutritional disturbances, too, are of great importance. It is very doubtful whether a primary cavity ever heals (Beitzke<sup>25</sup>).

**Lymph Node Component of the Pulmonary Primary Complex.**—*The Lymphatic System of the Lung*—Except for a narrow zone around the periphery which drains towards the pleura the lymph flow of the lung is

directed towards the hilus (W. S. Miller<sup>20</sup>). The lymph is collected in a fine intervalveolar net to be carried to larger vessels which follow the bronchi and blood-vessels in their course to the hilus. Some of the lymph vessels are also located in the interlobular septa. The first lymph nodes are inserted inside the lungs. They are the pulmonary lymph nodes which are found along the

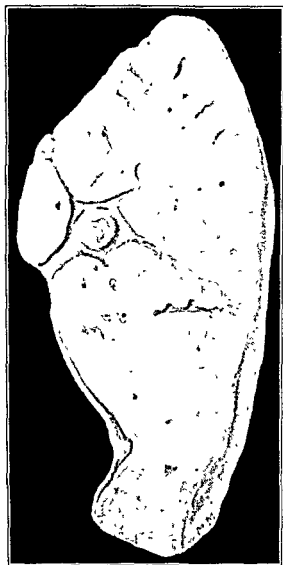


Fig. 9.—Lobar caseous pneumonia of the left upper pulmonary lobe, developing from a primary lesion. White male child, aged 3 years. Duration of illness 4 months.

bronchi and the branches of the pulmonary arteries. The next group of lymph nodes is situated between the first branches of the right and left main bronchus. These lymph nodes which are called the bronchopulmonary or hilus lymph nodes receive the lymph chiefly from the upper lobes but also some of the lymph from the middle and lower lobes. The main part of the lymph of the middle and lower lobes goes to a group of lymph nodes which fills the angle

of the bifurcation of the trachea and is larger on the right side than on the left side. This group has been designated as bifurcation lymph nodes. An important group of lymph nodes, the tracheobronchial nodes, occupies the space between the trachea, the superior vena cava, the innominate artery and the aortic arch. It is supplied mainly from the upper lobes. Recently these nodes have been called the lateral mediastinal lymph nodes. They are connected with the lymph nodes in the anterior and posterior mediastinum and with a chain of lymph nodes which follows the trachea upwards (paratracheal lymph nodes) and, in turn, is linked with the medial supraclavicular lymph nodes. From the lateral mediastinal lymph nodes a chain of nodes also extends along the innominate veins to the angle between the jugular and subclavian veins. The lymph nodes at the venous angle are of particular significance since they are the last filter station before the lymph enters the blood stream. The posterior mediastinal lymph nodes, finally, are connected with the celiac lymph nodes which surround the celiac axis. All these lymph nodes are linked by numerous anastomosing lymph vessels which show great individual variations and, especially the right lateral mediastinal lymph nodes are sometimes very severely affected in cases in which the primary pulmonary lesion is located in the left lower lobe. For further details on the thoracic lymph nodes reference is made to the publications of Ghon,<sup>12</sup> Beitzke,<sup>27</sup> St. Engel,<sup>28</sup> Sukiemikow<sup>29</sup> and Most.<sup>30</sup>

**The Spread of Pulmonary Infection to Regional Lymph Nodes.**—The studies on very recent pulmonary primary lesions indicate that the regional lymph nodes become infected very early (Ghon and Roman,<sup>31</sup> Ghon and Pototschnig<sup>32</sup>). In the lymph nodes too, the first changes are alterative and exudative and their further course is characterized by a rapidly progressing, massive caseation which may involve the entire lymph nodes. The question whether one is dealing with a primary tissue necrosis or with the caseation of specific granulation tissue is still under discussion and, especially, Huebschmann<sup>1</sup> stresses the predominance of the primary tissue necrosis. The closer the lymph node to the pulmonary focus the more marked is undoubtedly this primary tissue necrosis and epithelioid cell tubercles are scanty. With increasing distance from the pulmonary lesion the productive, specific changes become more and more marked except for the cases of rapidly progressing infection in which the primary tissue necrosis dominates the histological picture throughout. The spread of the infection may come to a standstill in the first filter stations, in the pulmonary, lateral mediastinal or bifurcation lymph nodes, or the infection may creep from one group of lymph nodes to the next group until it reaches the nodes at the venous angle and the danger of invasion of the blood stream becomes imminent. Subsidence of the spreading is brought about by the formation of a fibrotic, hyaline capsule about the caseated center which is supplied by the peripheral epithelioid cell tubercles and the capsule of the lymph nodes. The caseated center later becomes inspissated, calcified and petrified. The calcified center may finally become invaded, broken up and resorbed by granulation tissue and, when the resorbing granulation tissue changes into lymph adenoid tissue, the lesion in the lymph node may

disappear completely (Beitzke<sup>23</sup>). Ossification, however, is rare as compared to its frequency in old pulmonary primary lesions.

The lymph vessels between the pulmonary focus and the lymph nodes along which the infection travels show characteristic changes. At first, they are dilated and are filled with small round cells and large, mononuclear and phagocytic

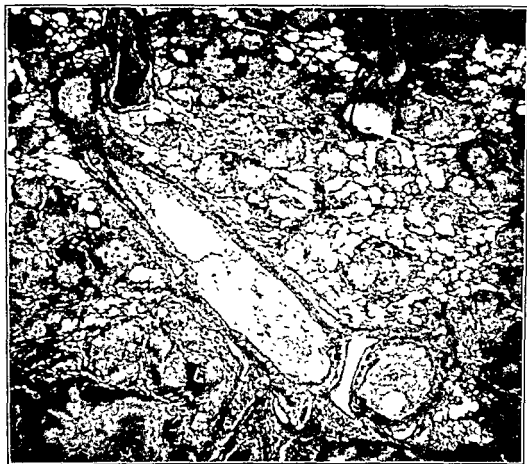


Fig. 10.—Aspirated caseous material in a bronchus of the right upper pulmonary lobe with acinous dissemination about the bronchus. The section is taken from the lung of a colored female child, aged one year. There was a partially calcified primary lesion in the left lower lobe and a massive caseation of the right tracheobronchial lymph nodes. One of the lymph nodes had perforated through a pinhead-sized opening into the main bronchus of the right upper lobe. Van Gieson stain, X 20.

cells. Later, the connective tissue about the inflamed lymph vessels becomes edematous and infiltrated by round cells and also typical epithelioid cell tubercles may be formed along the lymph vessels. These infiltrative and proliferative changes lead to a thickening and induration of the peribronchial and perivascular connective tissue.

When a pulmonary primary lesion lies very close to the pleura the tubercle bacilli may be carried with the lymph stream to the pleural lymph vessels and small tubercles may appear in the pleura over the primary lesion (W. S.

Miller<sup>26</sup>). The infection then extends to the small pleural lymph nodes, but later too, reaches the hilus lymph nodes.

*Perifocal Reactions.*—About the lymph node component of the pulmonary primary complex perifocal reactions take place which often are much more marked than the perifocal changes about the pulmonary lesion. They consist of an edematous loosening and of round cell infiltration, and in the later stages, of a fibrotic thickening of the capsule and the pericapsular tissue.

Extensive perifocal reaction about the lymph nodes at the hilus leads sometimes to a massive infiltration of the adjacent lung tissue (epituberculosis). This massive infiltration is exudative and transient although it may persist for many months. When the perifocal reaction about the primary lesion in the lung fuses with that about the lymph nodes at the hilus the entire lobe may become consolidated. During the process of clearing of the perifocal infiltrations the persisting shadows of the primary lesion and of the lymph node component give rise to the characteristic dumb-bell opacities on x-ray examination.

Ranke<sup>9</sup> attributes much significance to the perifocal inflammatory irritation of the bronchi which lie in close proximity to tuberculous lymph nodes. He speaks of a "hilus catarrh" which under certain conditions may cause massive atelectasis of a lobe by blocking the bronchus with mucus.

Intensive perifocal reaction about caseated hilus or bifurcation lymph nodes may be followed by an indurating fibrosis. There are cases in which this induration of the periglandular tissue is so marked that it causes stenosis of the bronchi or constriction of the veins at the hilus. The perifocal fibrosis may also fix the lymph nodes to adjacent structures, in particular to the trachea, the bronchi or the veins, thus preparing the way for a later perforation of the caseated nodes into these organs. When a caseated lymph node breaks into the trachea or a large bronchus, so much material may be aspirated that sudden death from asphyxia results. In other cases the massive aspiration leads to a rapidly progressing, pulmonary tuberculosis (Fig. 10). When the perforation into the bronchus is small and the caseous content of the lymph node is discharged gradually the caseous material may be expectorated and not aspirated and a small "bronchial lymph node cavity" is formed. Kolisko refers to aneurisms of branches of the pulmonary artery which develop occasionally in these cavities and which may cause a sudden and unexpected, fatal hemorrhage in an apparently perfectly healthy individual.

In rare instances a caseated lymph node may break into a pulmonary vein and lead to an acute miliary tuberculosis. The fixation of a lymph node to a pulmonary vein by perifocal fibrosis is often followed by a local coal pigmentation of the intima of the vein at the point of attachment.

## PULMONARY CHANGES IN EARLY GENERALIZATION.

### (II. Stage of Generalization, Ranke's Classification.)

The generalization that follows immediately the primary complex may be brought about in different ways. The dissemination by aspiration from an ulcerated pulmonary primary lesion or from a caseated lymph node which has perforated into the trachea or into a bronchus has already been referred to



Since this form of generalization uses the air passages it can be termed as "intracanalicular." The spread may also follow the lymph stream. The most important form of generalization, however, is hematogenous which results from the invasion of the blood stream by the tubercle bacilli.

It is, of course, very difficult to decide whether in every case of tuberculous primary complex the tubercle bacilli gain entrance into the blood stream. Provided the resistance is high, the number of bacilli small and the invasion of the blood stream of only short duration the body may be able to get rid of the bacilli, through the phagocytic activity of the reticulo-endothelial cells of the blood forming organs. Whether this is really the case remains to be proven. If the conditions are such as to allow the colonization of the bacilli the infection of the blood stream manifests itself in different forms. At autopsy, one finds occasionally, besides a fibrocaseous, calcareous or petrified primary complex, single more or less fibrosed, miliary tubercles in the spleen, the liver, the kidneys, lungs or other organs. These scanty, productive tubercles are usually of little significance. They heal and leave only a small hyaline or calcific nodule. But it is also from these isolated, hematogenous tubercles that the chronic, progressive tuberculosis of a single organ may develop in later life.

From the scanty, small productive, hematogenous tubercles a continuous series of changes lead to the typical acute miliary tuberculosis. The severe and rapidly fatal forms of generalization are due to a massive invasion of the blood stream and to a breaking down of the resistance which causes a high susceptibility to the tubercle bacilli and their toxins. They follow the caseation of the lymph nodes at the venous angle or the perforation of a caseated lymph node into a vein. In both instances the bacilli are carried to the lungs which are always severely affected. The lungs are distended, heavy and congested and on the pleural and sectioned surfaces one sees numerous, light yellow gray, caseous areas with irregular outlines which, because of the intensive perifocal reaction, are not sharply demarcated. The areas are usually largest in the upper lung fields, decreasing in size towards the base. They may be millet seed sized or smaller or they may fuse together to compact, caseated nodes several millimeters in diameter. In some instances they are surrounded by or contain foci of emphysematous lung tissue. The larger nodes may become liquefied and multiple small cavities may be formed. Microscopic examination reveals many focal areas of caseous pneumonia. The smallest foci are restricted to a few alveoli while the larger foci may correspond to one or several acini. In sections stained for elastic fibers one sees often in the center of the caseous areas a small bronchiolus (Huebschmann<sup>1</sup>). It is from the obstruction of the bronchioli by the caseous exudate that the occasional, localized, peri and intrafocal emphysema results (Pagel<sup>12</sup>). Around the alveoli filled with the caseous material there is a zone in which the alveoli contain a sero-sanguinous exudate. In these very severe forms productive changes are usually absent or one finds only a few epithelioid cells or an occasional giant cell in the periphery of the caseous pneumonic foci. In the subacute and chronic forms of hematogenous generalization, that means in the cases of higher resistance, the productive character is more marked and the miliary nodules consist chiefly of epithelioid cells with a small caseous pneumonic

area in the center. According to my experience, the productive miliary tuberculosis is less common than the exudative in early generalization.

*Intimal Tubercles.*—Tubercle bacilli often become lodged in the intima of the pulmonary veins and small *intimal tubercles* are formed. In some cases the miliary intimal tubercles grow to large elongated caseous nodes which measure several centimeters in length. These intimal tubercles rest upon the internal elastic membrane and consist of a caseous center and a peripheral zone of epithelioid cells and giant cells. The nodes may completely obstruct the lumen of the vessel (obliterating tuberculous endophlebitis) or they may ulcerate into the lumen, thus adding to the dissemination of the bacilli. There are cases in which an intimal tubercle appears to be much older than the other hematogenous lesions. In these cases the intimal tubercle can be considered as the first hematogenous metastasis which, by ulcerating into the lumen, has become a focus of secondary dissemination. The intimal tubercles are to be separated from the lesions which affect the wall of the veins by extension from adjacent tuberculous processes and involve first the adventitia.

Intimal tubercles develop occasionally in arteries. Obstruction of the arterial lumen by the caseous nodule may cause anemic or specific caseous infarction. Finally, the tubercle bacilli may localize themselves in the intima of the thoracic duct and large portions of the duct may become destroyed by caseation. The tuberculosis of the thoracic duct too, may serve as a focus of secondary dissemination.

The severe and rapidly fatal forms of early generalization occur chiefly in infants and small children. In later life, they are rare. In the majority of the cases the pulmonary primary lesion is very large, often ulcerated without tendency to encapsulation. The involvement of the thoracic lymph nodes is most severe. I have taken from my records 97 consecutive cases of early generalization. All these cases were in children under 15 years of age. In 70 per cent. there was a tuberculous leptomeningitis. Seventy-two per cent. showed progressing, caseous pneumonic primary lesions of the lung without encapsulation. In half of these cases the primary lesion was ulcerated (primary cavity). In 24 per cent the primary lesion was fibrocaseous and in 4 per cent. it was fibrocalcereous.

## ISOLATED PULMONARY TUBERCULOSIS.

### (III. Stage of Isolated Tuberculosis, Ranke's Classification.)

*Pathogenesis.*—Concerning the origin of the isolated pulmonary tuberculosis two possibilities have to be considered; namely, one of the old lesions which have been left over from the primary stage or from an eventual early generalization may flare up and start to progress, or a new exogenous infection may affect the lung. This new, exogenous infection is termed better as superinfection than as reinfection since reinfection would mean the complete elimination of the effects of the first infection with the restoration of virgin conditions, which certainly is not true of the great majority of the cases of pulmonary tuberculosis of later



Plate I.—Caseous infiltration of the apical and subapical part of the right upper pulmonary lobe. Microscopically the area shows a diffuse caseation of the exudate and the alveolar walls and there are no epithelioid cells nor giant cells in and around this area. White male, aged 49 years. Cause of death acute pancreas necrosis. The history states weakness and loss of 20 lb during the last six months preceding the death. Hand colored photography.

life. For the flaring up of the old lesions "endogenous exacerbation" is the term of choice (Ghon).

The opinions of the different investigators as to the significance of the two possibilities are divided into two nearly equal groups, some regarding the endogenous exacerbation as the only solution of the problem of isolated pulmonary tuberculosis, others attributing little or no importance to it. It seems to me that both explanations have much in their favor, that both possibilities actually occur though perhaps the exogenous superinfection is of greater frequency and of greater importance than the endogenous exacerbation. It is, however, not up to the morbid anatomist to decide this question. He can merely discuss his observations in the light of the two theories and see which one fits best with what he observes at the autopsy table. Studies on the frequency of pulmonary tuberculosis in people with a known severe exposure as for instance those of Opie and McPhedran<sup>23</sup> on marital tuberculosis are much more important than even the most minute anatomical investigations. It is with this restriction in mind that the different explanations will be discussed from the standpoint of the morphologist.

(A) *Endogenous Exacerbation*.—Before quoting the lesions which might be responsible for an endogenous exacerbation it is necessary to say a few words about the persistence of living and virulent tubercle bacilli in old calcified and authors (Opie and Aronson,<sup>24</sup> Schrader,<sup>25</sup> Anders<sup>26</sup>). But granted even that one succeeds in demonstrating virulent tubercle bacilli in calcified nodules of the lungs or lymph nodes this demonstration is of but limited value since, after a calcified lesions of the primary complex than has been assumed by earlier longer stay in the hospital, tubercle bacilli are quite often found in parts of the lungs or in lymph nodes which are free from tuberculous changes (Opie and Aronson,<sup>24</sup> Hartfall and Thomson<sup>27</sup>). I think that the histological changes petrified tuberculous foci. Recent investigations have shown that, especially beyond the age of 40 years, living tubercle bacilli are much less common in the in the old lesions are more important than the bacteriological examination by culture or animal inoculation. It has been stated in a preceding chapter that, in later life, granulation tissue often invades and substitutes the calcareous centers of the primary lesion in the lung and of the lymph node component. In an histological study on a great number of old primary lesions of the lung I have been unable to record a single instance in which the invading granulation tissue revealed specific changes. If viable tubercle bacilli had still been present in the calcified centers tubercle formation would have occurred. The same holds true of the organization of calcified lesions in the lymph nodes. Siegen<sup>28</sup> stresses the fact that the encapsulated primary lesion of the lung is not completely separated from the body but that it is connected with the adjacent lung tissue by a connective tissue stalk with blood and lymph vessels. He believes that this connection may be of importance with regard to the exacerbation of a pulmonary primary lesion. There are, however, only very few observations on record in which the exacerbation of an old pulmonary primary lesion could be definitely proved.

In a classical series of studies Ghon<sup>30</sup> and his associates called attention to the exacerbation of the lymph node component of the primary complex. A bronchopulmonary, tracheobronchial, peritracheal or other thoracic lymph node was found to contain a calcified area and around it a crop of cascating tubercles, and from this node a chain of recent lesions led to the lymph nodes at the venous angle. Like other investigators (Schuermann,<sup>40</sup> Anders<sup>41</sup> and others) I have repeatedly been able to confirm Ghon's observations, but similar to Anders I have also obtained the impression that the endoglandular exacerbation was followed more frequently by extrapulmonary metastases (meninges, adrenals, bones, genitourinary organs) than by pulmonary tuberculosis.

During the early generalization single tubercles may be formed in the lung which later become calcified (monotypic, pulmonary metastases of an abortive secondary stage). Wurm makes the statement that these calcified foci of early generalization are three times as common in tuberculous lungs as in lungs which contain only the primary lesion, and that from 30 to 40 per cent. of the lungs with progressing tuberculosis reveal them. The calcified foci show also histological evidences of reactivation in form of infiltrations which spread by aspiration. The figures which Wurm gives for the calcified metastases of the second stage are unusually high but even with these high figures from 60 to 70 per cent. of the cases of isolated pulmonary tuberculosis do not show these signs of early generalization.

(B) *Exogenous Superinfection.*—As far as the exogenous superinfection is concerned its effect may be twofold. First, the inhaled tubercle bacilli may disintegrate without producing any local changes and from the disintegrating bacilli tuberculin like substances may be liberated which act upon the old, silent foci as a stimulant, inciting their reactivation, or the tubercle bacilli gain a foothold and lead to a new infection of the lung.\*

The most common anatomical site of the isolated tuberculous changes of the lung is the apex. Why is it that the superinfection affects mainly the apex while the primary lesion shows little affinity to it and selects the portions of the lung with the best respiratory ventilation? The isolated calcified nodules of the second stage are more common in the apex than in the other parts of the lung which would suggest that the apical lesions develop from the remnants of the second stage. On the other hand, one has to keep in mind that the primary lesion occurs most frequently in childhood whereas the superinfection is most common in adults. The mechanical and biological conditions in the lung in childhood cannot be compared with those in adult life. What holds true for disposing the apex of the lung to the metastases of the second stage, namely the compression by the first rib, the poor respiratory ventilation and the relatively sluggish blood circulation, may be applied also to superinfection. Thus, one can see that the anatomical findings may be well adjusted to one's particular conception.

\*Koch's fundamental experiment which shows that a superinfection does not lead to a progressive tuberculosis in a tuberculous guinea-pig but is followed by a quick reaction with complete elimination of the reinjected bacilli cannot be applied to human tuberculosis. In addition to many other factors which cannot be discussed here the number of tubercle bacilli eventually present in old tuberculous lesions is much too small as to prevent the take and progression of a sufficiently strong superinfection.

Before leaving the subject of pathogenesis reference should be made to the question whether the primary lesion has any effect upon the development of the isolated pulmonary tuberculosis. There can be little doubt that large, healed primary lesions of the lung are much more common in cases without pulmonary tuberculosis or in cases with a benign tuberculosis than in cases with a severe and ulcerative tuberculosis. It seems, therefore, that a strong primary reaction produces a certain increase in resistance of the lung to new tuberculous processes.

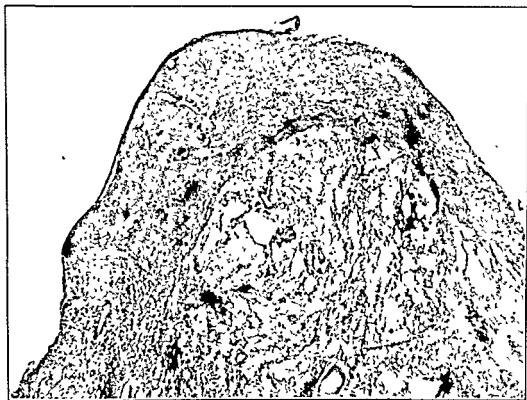


Fig. 11.—Apical, subpleural scar of the left upper pulmonary lobe. In the scar are a few areas of inspissated caseation which are surrounded by lymphocytes. The section is taken from the lung of a white man aged 68 years who died from a carcinoma of the stomach. X 6½.

Wucherpenning<sup>42</sup> found only in 7.5 per cent. of the cases with ulcerative tuberculosis the old primary lesion. It is, however, possible that in the course of a progressive tuberculosis the primary lesion may become obscured, especially by decalcification (Gräff<sup>43</sup>).

*Apical Lesions.*—Anatomically the apex of the lung is the portion of the upper lobe which is located above the first rib. It is a flat cap, only a few millimeters high (Van Nooten,<sup>44</sup> Pagel<sup>45</sup>). From the clinical point of view the apex is even smaller since the clinicians take the clavicle as the border and distinguish between the supra (apical) and infraclavicular territory. According to Anders<sup>45</sup> and Orsos<sup>46</sup> the geometrically highest point of the lung *in situ*, the "culmen," is located below the capitulum of the first rib since the apex is

inclined in ventromedian direction. This culmen of the lung is the most common site of the first postprimary tuberculous changes (Pagel<sup>15</sup>).

At autopsy scars are very frequently found in the apical portion of the upper lobes of the lungs (Fig. 11). These scars show a predilection to the territory of the dorsal, apical bronchiolus. They may be restricted to the pleura and a narrow subpleural layer of lung tissue, or they may extend deeper into the lung parenchyma, subdividing it often into emphysematous lobules. The pleural scars are firm, often of cartilage-like consistency. They may or may not be associated with adhesions to the wall of the chest. The deeper scars consist of dense, anthracotic connective tissue, which, in a considerable percentage of the cases, contains inspissated, caseous nodules. In some instances the apical scars are so small that they can be detected only by microscopic examination.

It is a much discussed question whether all these scars are really the result of a tuberculous superinfection or whether nonspecific indurative processes lead to similar changes. If one answers this question in an affirmative sense superinfections are just as common as the primary lesions (Schmincke,<sup>47</sup> Gräff,<sup>48</sup> Anders,<sup>49</sup> Loeschke,<sup>50</sup> Aschoff,<sup>51</sup> Focke<sup>52</sup>). Lubarsch,<sup>53</sup> Schuermann,<sup>54</sup> Oberndorfer,<sup>55</sup> Rabl<sup>56</sup> and others, however, believe that one is not justified to call every apical scar tuberculous. I could convince myself that the majority of the grossly noncharacteristic scars showed sufficient microscopic evidences in favor of their tuberculous origin (see also Focke<sup>52</sup>).

The apical scars increase in frequency after puberty. Aschoff's pupil Puhl<sup>57</sup> calls attention to a well defined type of apical scar which he believes is very characteristic of an exogenous superinfection. These "Puhl's lesions" are quite different from the primary lesions. They consist of from two to five dense caseous nodules which are surrounded by a specific, hyaline and a thick, non-specific, fibro-anthracotic capsule. Ossification is rare and there is no lymph node component, which is perhaps the most important difference from the primary lesion. Aschoff states that there may be several successive superinfections. The more recent ones showing the tendency to a subapical location.

Puhl is convinced that all these lesions are exogenous in origin. Some observations, however, indicate that the miliary dissemination of the early generalization may be restricted to the apex, that there are cases in which the infection of the blood stream manifests itself anatomically only in this portion of the lung. Simon<sup>58</sup> describes apical caseous and calcareous nodules which can be found already in small children and which develop soon after the primary lesions (subprimary). The nodules are hematogenous and harmless since they do not tend to progress. W. Neumann's discrete miliary tuberculosis (*miliaris discreta*) is apparently related to the Simon's foci. Pagel<sup>15</sup> concludes, therefore, that many of the apical lesions are hematogenous metastases.

Whether endogenous or exogenous the apical lesions are at first exudative-caseous in character. The small acinous foci of caseous pneumonia soon become overshadowed by proliferative changes. Walls of epithelioid cell tubercles are built and, together with the fibrocytes of the surrounding tissue, the tubercles produce dense scars. These changes demonstrate that the infection takes place in a highly resistant organism. But may these apical lesions, under certain con-

ditions, also lead to a progressive pulmonary tuberculosis? With this question we enter upon another much disputed field.

The French investigators, and with them W. Neumann,<sup>59</sup> consider the apical processes as the result of abortive tuberculous infections. The majority of the morbid anatomists insist that the progressive pulmonary tuberculosis starts in the apex (Aschoff, Graeff, Loeschke, Huebschmann and others). They admit that the great majority of the apical lesions heal anatomically. But some of them progress, either from the beginning or later by exacerbation, gain connection with a bronchus, break into the lumen of the bronchus and thus open the way for a dissemination by aspiration.

The great progress of recent years in the roentgenological detection of the early stages of the progressive pulmonary tuberculosis has diverted the interest from the apex to the infraclavicular region (Assmann,<sup>60</sup> Redeker,<sup>61</sup> Braeuning,<sup>62</sup> Romberg,<sup>63</sup> Ulrici,<sup>64</sup> Douglas, Pinner and Wolepor<sup>65</sup> and others). It is in the infraclavicular region that the progression first becomes demonstrable. Hence, pathologists too, are beginning to concentrate their attention upon the infraclavicular infiltrations.

*Infraclavicular Infiltrations.*—Anatomically, the infraclavicular infiltrations are tuberculous processes, chiefly exudative in character, which follow the sub-apical bronchi of the upper lobes. Productive changes are insignificant or absent. There are confluent acinous areas of caseating exudation alternating with areas in which the alveoli are filled by large mononuclear cells (alveolar phagocytes), by fibrin or a sero-sanguineous material. These later changes represent perifocal reactions. The caseous pneumonic areas are very apt to become liquefied and quickly to change into cavities which, by aspiration, lead to a rapid dissemination to the other portions of the lungs. The infraclavicular caseous foci may also escape ulceration and become encapsulated. Though temporarily silent, they are, however, always ready to flare up if decrease in resistance favor their progression. The encapsulation is usually brought about by a nonspecific organization of the exudate which forms the perifocal reaction.

When recognized early and treated properly the infraclavicular infiltrations may clear up completely. About the anatomical nature of these transient infiltrations little is known but it is most likely that the exudate becomes resorbed before caseation sets in. It is also possible that the shadow on the x-ray plate is produced by extensive perifocal reactions about cheesy nuclei too small to be visible after the perifocal reaction has disappeared.

Since apical lesions are so common they are also found in the majority of the cases with infraclavicular infiltrations which come to autopsy. Regarding the relations between the apical lesions and the infraclavicular infiltrations, three possibilities are to be considered. First, by progression the apical lesion may lead to the infiltration in the infraclavicular region. Second, the apical lesion may be completely healed and the infraclavicular infiltration may be due to a new, independent superinfection. Aschoff states that in the presence of apical scars new infections tend to select deeper portions of the lung. Finally an infraclavicular infiltration may disseminate into the apex.



Careful histotopographic studies of Loeschcke,<sup>66</sup> Schuermann,<sup>67</sup> Pagel<sup>15</sup> and others have shown that the apical lesions are an important, if not the most important, source of the infraclavicular infiltrations (see also Aschoff<sup>68</sup>). According to Loeschcke the upper lobe has three dorsal and four ventral bronchi. For the progression of the tuberculosis the dorsal bronchi are of greatest significance. These three dorsal bronchi are: the apical, the subapical and the horizontal bronchus. The apical bronchus supplies the apex proper, the subapical bronchus branches off into the dorso-lateral part of the subapical region

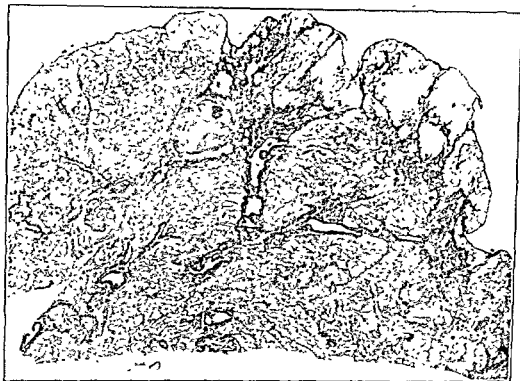


Fig. 12—Coarse shot-like dissemination in the region of the apical, subapical and horizontal bronchus of the left upper pulmonary lobe. There are two older fibro-caseous nodules which are connected with small bronchi. The section is taken from the lung of a white male aged 25 years who came to death from a chronic glomerulonephritis. Weigert's elastin stain X 5

while the dorsal part of the upper lobe above the interlobar fissure receives its branches from the horizontal bronchus.

As pointed out in the preceding chapter the apical lesion starts as a small intra-acinous focus of caseating exudation. When it progresses it descends into the afferent bronchiolus which is a branch of the apical bronchus. A caseating endobronchiolitis develops and the exudate trickles down in the lumen till it reaches the first bifurcation. The passing air current breaks off some of the infectious material which, with the next inspiration, is carried into an adjacent area. New small intra-acinous foci are formed which are productive (small shot-like dissemination). This fractional dissemination may go on in caudal direction and crop after crop of small productive tubercles appear.

In the case of rapid progression of the apical lesion the caseating endo-bronchiolitis spreads by continuity into the main apical bronchus the lumen of which becomes filled by a plug of caseous material rich in tubercle bacilli (caseous bronchial thrombus, Loeschcke). From the apical bronchus the caseous material is aspirated into the subapical and horizontal bronchus and, since the aspiration is massive, confluent areas of caseous pneumonia result (coarse shot-

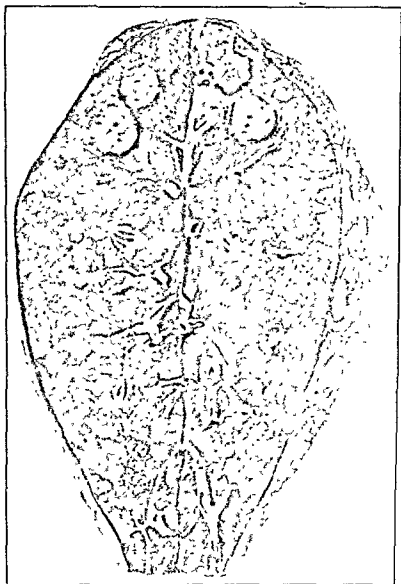


Fig. 13.—Subapical round caseous pneumonic foci of the left upper pulmonary lobe. See also the microphotographs Figs. 4 and 14. White female, aged 36 years. Endoglandular tuberculous exacerbation in the lymph nodes at the hilus of the right lung with diffuse spreading to the tracheo-bronchial, mediastinal, peripancreatic and periaortic lymph nodes. Bilateral tuberculous salpingitis and single miliary tubercles in the spleen, liver and kidneys. Calcified primary lesion in the right middle pulmonary lobe. Terminal endocarditis of the mitral valve. Petechiae of the skin. Severe anemia from continuous vaginal bleeding.

like dissemination) (see Fig. 12). It is this coarse shot-like dissemination which produces the infraclavicular infiltrations (Loeschcke). As long as the process is restricted to the dorsal bronchi it may heal. Extension to the ventral bronchi makes healing much less probable.

I have repeatedly been able to confirm Loeschcke's important observations. It may be added that the process of endobronchitic dissemination which leads to the infraclavicular infiltrations starts sometimes from a subapical focus found

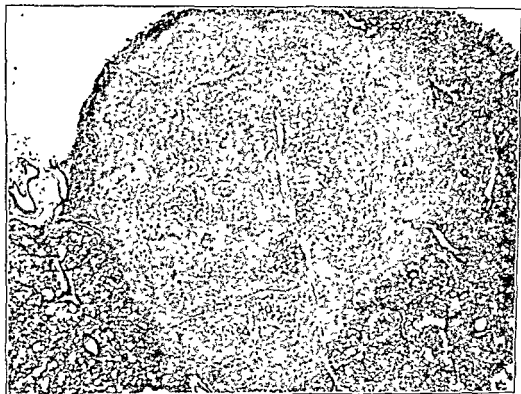


Fig 14—Round focus of caseous pneumonia (see also Figs. 1 and 13). Note the sharp demarcation of the pneumonic area from the surrounding lung tissue, X 10.

beside an old apical scar. Between superinfection and progression there may be a long interval and even calcified foci may flare up and break into adjacent bronchi.

There are cases with apical scars and infraclavicular infiltrations in which even serial sections fail to reveal connections between the scar and the recent lesion. In these cases the infraclavicular infiltration has to be considered as due to an independent superinfection. Pagel,<sup>69</sup> Elias,<sup>70</sup> Kudlich and Reimann<sup>71</sup> and others described early infraclavicular infiltrations in which no apical lesion could be found. In this connection it may be mentioned that the apex may take part in the formation of the early infiltration and that the caseating process may involve both apex and infraclavicular region to the same extent so that one cannot decide whether the apical focus has disseminated into the infraclavicular region or *vice versa* (see Color Plate I).



Plate II.—Chronic ulcerative tuberculosis of the right upper pulmonary lobe and confluent gelatinous and caseous pneumonia of the lower lobe. Colored female, aged 56 years. Duration of illness unknown, but during the last two months rapid progression. Hand colored photograph.

Loescheke<sup>66</sup> and with him the majority of the morbid anatomists see the only source of the infraclavicular infiltrations in an exogenous, post-primary superinfection. Pagel,<sup>15</sup> however, stresses the fact that hematogenous metastases to the lung may assume the appearance of early infraclavicular infiltrations and I think that he is right. I am referring particularly to the round foci which have been described by Albert, Lachmann, Straub<sup>72</sup> and others. These round foci which are undoubtedly hematogenous, are single or multiple and show a predilection to the infraclavicular region. They consist of a circumscribed area of caseous pneumonia with little reaction about it (Figs. 13 and 14, see also Fig. 1). This area is surrounded by a capsule of connective tissue and the center may be partially or completely calcified. There is no involvement of the regional lymph nodes. Clinically the round pulmonary foci cause no symptoms. There is no fever, the sputum is free from tubercle bacilli and the sedimentation rate of the erythrocytes is not increased. The foci are discovered incidentally on the chest plates as sharply circumscribed round shadows resembling metastases of a malignant tumor. X-ray pictures taken several months or even from one to two years later disclose that the size and shape of the foci have remained stationary. This inactivity and stability distinguishes the round foci from the infraclavicular infiltrations which are characterized by being very labile. The round foci may, however, become activated, they may break down and produce cavities or they may progress by centrifugal growth and reach a bronchus. The picture which results is identical with a typical infraclavicular infiltration. Finally small calcified metastases of the secondary stage in any part of the lung may become activated, break into a bronchus and disseminate into the infraclavicular region (Pagel, Schmincke). This holds true, especially, for the endogenous pulmonary tuberculosis of puberty.

### PROGRESSIVE PULMONARY TUBERCULOSIS.

(A) *Acinous-Nodose Tuberculosis*.—The acinous-nodose tuberculosis is the anatomical substratum of the chronic, slowly progressing tuberculous infection of the lung which spreads in cranio-caudal direction along the air passages. The structure and mode of infection of the pulmonary acinus have been discussed previously.

To the naked eye the acinous lesion presents itself as a pinhead to pea-sized nodule with scalloped edges which is attached to a fine stalk like a grape. This stalk is formed by the afferent bronchiolus and arteriole. Because of the perifocal reaction the recent nodules are not sharply separated from the adjacent lung tissue. When the lesions grow older and the perifocal reaction subsides the nodules are distinctly raised over the sectioned surface and feel firm. The center is either caseous or sclerotic anthracotic. The periphery shows pearly gray or yellowish gray secondary nodules. The acinous lesion increases in size by continuity, the process breaking into neighboring acini, or by fusion of, at first, separated nodules. Thus, nodes result which measure up to 4 and 5 centimeters in diameter.

The chronic character of the acinous-nodose tuberculosis is due to the fact that the lesions are chiefly productive in nature and reveal a great tendency to scarring. The scarring starts in the center of the lesions. It seems to originate from the broncho-vascular stalk and the stagnating lymph flow in the sclerosing connective tissue leads to the piling up of much coal pigment. In the periphery the lesions progress with the formation of new tubercles which later, too, change into scar tissue. Ultimately the whole lesion may become transformed into a deeply pigmented scar which is surrounded and more or less obscured by emphysematous lung tissue. Under certain conditions, however, the sclerosing character of the lesions gives way to a rapidly progressing caseation which is followed by liquefaction. By rinsing the sectioned surface with a gentle stream of water, plugs of caseous pus are then washed out from the center of the lesions which now appear as small, irregular cavities lined by shaggy, caseous granulation tissue (Fig 15).

Microscopically the young acinous lesion consists of an irregular caseous area which is encased in a wall of epithelioid cells. The epithelioid cells are usually arranged radially about the caseous center. They seem to stream towards the center, their nuclei assuming a long drawn out and often tortuous shape. The number of giant cells varies. In the young foci they are often numerous, while in the older foci they are scanty. Around the wall of epithelioid cells there is a zone of granulation tissue with many small round cells, fibrocytes and circumscribed, round tubercles. In the later stages much collagenous ground substance is deposited which replaces the caseous center as well as the capsule of epithelioid cells and granulation tissue. The afferent respiratory or, in the larger lesions, terminal bronchiolus is filled with a caseous exudate about which the wall of the bronchiolus becomes transformed into specific granulation tissue. It is from the caseous content in the bronchiolar lumen that infectious material is aspirated into adjacent acini.

Huebschmann<sup>1</sup> emphasizes that the acinous lesion starts as a focal caseous pneumonia and that the epithelioid cell reaction is secondary to it. Nicol<sup>4</sup> and others consider the acinous lesion as productive from the beginning, the caseation involving the specific granulation tissue. For the majority of the cases Huebschmann's explanation holds true though the initial exudative caseation may be insignificant as compared to the caseation of the tubercles formed about it. In very chronic cases the productive changes dominate the microscopic picture throughout.

Between closely adjacent acinous and acinous-nodose lesions the lung tissue becomes compressed, atelectatic and indurated. Perifocal induration may also result from the nonspecific organization of the exudate of the perifocal inflammation. These scars, too, are dense and anthracotic and fuse with the scars derived from the acinous lesions themselves. In the scars single alveoli are often enclosed which have lost the connection with the bronchial tree. These isolated alveoli are lined by a cuboidal epithelium which I think is derived from the epithelium of the respiratory bronchioli.

Prior to the recognition of the intracanalicular, acinar spread of the infection by Aschoff and Nicol the type of tuberculosis under discussion had been called



Plate III.—Thin walled, punched out cavity in the infraclavicular region of the left upper pulmonary lobe. About the cavity multiple small areas of caseous pneumonia. In the apex a small anthracotic-fibrotic scar. White woman, aged 45 years. Cause of death: chronic encephalitis. No clinical manifestations of the tuberculous process. Hand colored photography.

peribronchial because it was thought that the infection traveled in the lymph vessels around the bronchi and extended into the adjacent alveoli by continuity. Peribronchial tubercles do occur in acinous tuberculosis but they are secondary to the involvement of the alveoli.



Fig. 15.—Productive, acinous-nodose tuberculosis of the right upper pulmonary lobe. There are multiple small cavities which originate from the caseous centers of the conglomerate tubercles and are lined by epithelioid cells and giant cells. Between the nodose lesions the lung tissue is atelectatic and indurated and the interlobular septa are thickened. In the left upper corner there is a subpleural scar. The section is taken from the lung of a white male, aged 51 years. The break in the resistance which accounts for the liquefaction of the nodose, productive tubercles can be attributed to persistent bleeding from a chronic peptic ulcer of the stomach. X 3.

(B) *Caseous Pneumonia*.—In the discussion of the primary lesion of the lung and of the pulmonary manifestations of the early generalization the great significance of exudative, caseous changes has been emphasized. It has also been pointed out that in the majority of the acinous-nodose lesions of the tertiary



stage the productive processes are preceded by an initial caseating exudation. In some forms of the isolated pulmonary tuberculosis which are apparently the result of a high susceptibility and of a lack of resistance the initial exudation is not checked by the specific productive response and the exudation progresses and determines the anatomical picture. The mode of infection and dissemination



Fig. 16—Confluent caseous pneumonia of the right lower lobe. In the lymph node bulging into the lung there is a calcified area. Colored male aged 26 years. Duration of illness six months

is the same as in the productive type of pulmonary tuberculosis. The tubercle bacilli are aspirated into the alveoli, set up a local tuberculous inflammation from which the process spreads to the afferent bronchiolus which, in turn, becomes the source of new aspiration foci.

At first small and involving only part of an acinus the exudation may spread rapidly, progressing beyond the acinus and beyond the lobulus and leading to large, confluent infiltrations (Fig. 16) which may terminate into the massive

consolidation of an entire lobe (caseous lobar pneumonia). In the early stages the pneumonic areas are glassy, translucent and light gray or purple gray in color. The sectioned surface is smooth and yields a small amount of viscid, cloudy fluid (gelatinous pneumonia). On microscopic examination the alveoli are found filled with a pale stained, homogeneous material which contains many alveolar phagocytes stuffed with lipoid droplets and a smaller number of leukocytes, lymphocytes and erythrocytes. Fibrin is absent and tubercle bacilli are scanty (catarrhal or desquamative pneumonia of the older authors). If the body regains quickly its resistance the process comes to a standstill with the cellular, serous exudation, the exudation is resorbed and normal conditions are restored. If this is not the case, the exudate becomes rich in fibrin, the cells disintegrate and the alveolar septa break down. The pneumonic areas now are firm and dry and light yellow gray in color. About the caseous pneumonic areas the perifocal reactions are usually much more marked than about the acinous-nodose, productive lesions and, because of the expansion of the coagulating and caseating exudate, there is also a zone of compression atelectasis around the pneumonic foci.

With further increase in susceptibility the tubercle bacilli multiply rapidly and the caseous material impregnated with their toxins attracts a great many polymorphonuclear leukocytes. The dry, caseous consolidated areas become perforated by many small foci of liquefaction and suppuration which fuse together and lead to the formation of cavities lined by the remaining caseous material. Aspiration from these liquefied pneumonic areas is most extensive and soon affects the parts of the lung which are still functioning (galloping type of pulmonary tuberculosis). Hemorrhages into these cavities are rare, unless the liquefaction of the caseous foci progresses very rapidly. This is due to the fact that in the pneumonic areas the blood-vessels become obliterated either through an edematous swelling of the wall and a proliferation of the intima (Fig. 17) or through a caseous coagulation of the column of blood in the lumen of the vessels (Konschegg,<sup>73</sup> Pagel<sup>12</sup> and others).

The caseous pneumonic process, however, may also become arrested, indicating that the body has passed successfully through the period of lowered resistance. The arresting is brought about by a fibrous encapsulation or replacement of the caseous foci. It is interesting that in the productive processes about the caseous pneumonias specific granulation tissue plays an insignificant rôle or is completely absent. Namely, the scar tissue is derived from the preëxistent connective tissue of the interlobular septa and about the blood-vessels and bronchi, and from the granulation tissue which organizes the exudate of the perifocal inflammation. In van Gieson stained sections of caseous pneumonic areas one sees often islands of intact purple red connective tissue in midst of the light yellow brown necrosis. These islands supply the bulk of the scar tissue which may ultimately replace the whole caseous area (Huebschmann<sup>4</sup>). Some of the smaller encapsulated caseous pneumonic foci may become calcified, but ossification does not occur.

(C) *Indurative Tuberculosis*.—It may, perhaps, be questioned whether one is justified in speaking of the indurative pulmonary tuberculosis as a special

form of the disease since, as pointed out in the preceding chapters, the indurative processes are merely the eventual outcome of the productive or exudative tuberculous inflammation. The scarring and induration do not really belong to the tuberculosis itself but are the result of successful attempts at healing. But in spite of its great tendency to heal the indurative tuberculosis creeps slowly from one part of the lung to another and leads finally to severe changes in the



Fig 17—Obliterating endarteritis in an area of caseous pneumonia.  
Weigert's elastin stain, X 300

anatomical structure and functional capacity of the organ, interfering greatly with respiration and pulmonary circulation and causing death indirectly.

Biologically the indurative type of the tuberculosis indicates a high resistance against the infection. Complicating diseases, such as diabetes mellitus, leukemia, malignant tumors, often depress the resistance and the indurative tuberculosis changes into the acinous-nodose or ulcero-caseous form.

Though most frequent in advanced age the indurative tuberculosis is observed occasionally also in young individuals and even in children. The acinous-nodose, productive or the sublobular and lobular exudative-caseous lesions are gradually transformed into a firm and deeply pigmented scar tissue which replaces the normal alveolar structure, and indurative atelectasis and

organization of the exudate of the perifocal reaction help in spreading the process over large areas of the lung. The scar tissue often maintains the nodular arrangement of the epithelioid cell tubercles and here and there a small remnant of the caseous material may be encountered. Epithelioid cells are scanty and giant cells of Langhans type are absent. The giant cells which are occasionally found are of the foreign body type.

The sequelæ of these indurative changes are diffuse and saccular bronchiectases, compensatory emphysema of the portions of the lung that have escaped the fibrosis and great reduction of the vascular bed of the lung. The bronchiectases may become the site of secondary, nonspecific, suppurative and ulcerative processes. The epithelium which lines the bronchiectases may change into transitional or squamous epithelium which may become the point of origin of a carcinoma. The emphysematous blebs may burst and cause a pneumothorax. The reduction of the vascular bed of the lung increases the resistance to the blood flow from the right ventricle of the heart which, in younger individuals, is able to compensate by hypertrophy of its wall. The reserve power of the right ventricle may finally become exhausted and the patients die from an insufficiency of the right heart.

In recent years much attention has been given to the relations between silicosis and tuberculosis, and silicosis has been found to increase the disposition of the lung to progressing tuberculosis. There is a type of pulmonary silicosis which is characterized by the formation of very hard and deeply pigmented nodules and nodes which are very similar to those seen in indurative tuberculosis.\* The old pathologists (Rokitansky, Rindfleisch, Ribbert and others) identified all silicotic-fibrotic nodules of the lung with indurated tubercles, a conception which is also found among modern authors (Ickert<sup>74</sup> and others). Husten<sup>75</sup> believes that the nodose type of silicosis is always tuberculous. It seems, however, that quartz dust is able to produce sclerosing granulomas and that tuberculosis is not a necessary prerequisite of the nodose, pulmonary silicosis (Giese<sup>76</sup>).† It is an interesting and not yet fully explained phenomenon that the silicotic nodules may undergo liquefaction and become transformed into cavities very similar to old tuberculous cavities (Gerlach<sup>77</sup>). The fluid in these cavities is sterile.

(D) *The Tuberculous Cavity*.—Although cavities in the lung were already known to the Hippocratic school of medicine, De le Boe Sylvius (17th century) and Laennec (early part of the 19th century) were the first to associate them with tuberculosis (W. Pagel<sup>15</sup>). Laennec defined the pulmonary cavity as the result of the liquefaction of a large area of tuberculous matter. At the beginning of the histological epoch it was thought that the material between the tubercle cells became liquefied and that the tubercle cells changed to pus cells. At present

\* The microscopic differentiation between simple fibrotic tubercles and silicotic tubercles is often difficult. In these cases microincineration of the sections which allows the demonstration of the quartz crystals in polarized light is of great help.

† Good pathologic-anatomic discussions on the relations between silicosis and tuberculosis are found in the publications of Mavrogordato, A. (South African Int. Med. Res. Rep., 19, 1926); Policard, A. (Presse Medical, page 80, 1932, and page 5, 1933); Belt, J. H. (Can. Publ. Health Journ., 20: 494, 1929); and Gardner, L. N. (Amer. Rev. Tuberc., 29: 1, 1934).

the liquefaction is attributed to the proteolytic action of immigrating leukocytes. In the region of the liquefaction the bronchioli and small bronchi are destroyed while the larger bronchi become the outlets of the accumulating pus. By carrying the infection to other parts of the lung, to the upper respiratory tract, the oral

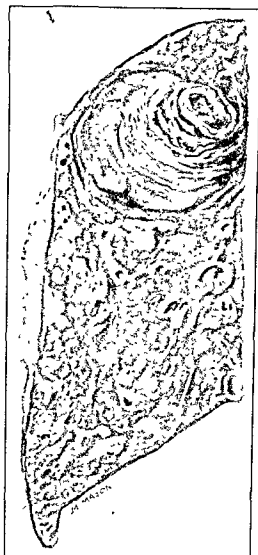


Fig. 18.—Fatal hemorrhage into a tuberculous cavity of the right upper pulmonary lobe. Note the laminated blood clots which surround the ruptured aneurism. Multiple foci of caseous pneumonia alternating with areas of aspirated blood throughout the lobe. White male, aged 25 years

cavity and the intestine, this bronchial drainage becomes the most serious sequela of the cavity formation.

From the discussion of the productive and exudative tuberculous changes given in the preceding chapters it is evident that both types of lesions may lead to cavitation. The exudative changes are, however, of much greater significance

and especially the large and rapidly developing cavities can be traced to them. The process of liquefaction starts with a softening of the caseous material by hydropic swelling of the cellular débris. Streaks of polymorphonuclear leukocytes force their way into the softened tissue and separate it into smaller pieces. The streaks and small lakes of pus fuse together, and soon the whole caseous focus is transformed into pus. This suppurative liquefaction stops at the border of the caseation. When productive acinous-nodose lesions are the site of cavity formation the granulation tissue about the caseous centers prevents at first the progression of the liquefaction. In the case of caseous pneumonia a wall of non-specific granulation tissue is built before the liquefaction reaches the border.

The tuberculous cavities show a predilection to certain parts of the lung. The peripheral, lateral and dorsal regions are the most favored sites. The apex of the lower lobes is more prone to become affected than the base of the upper lobe (W. Ewart). Since the macerating action of the pus upon the wall of the cavity is most intensive at the deepest points the cavities grow in caudal direction. Extension of a cavity from one lobe into an adjacent one is rare.

Depending upon the mode of formation and expansion and the changes in the surrounding lung tissue the size and shape of the cavities are subject to great variations. There are cavities which are only one to two centimeters in diameter and others which involve an entire lobe. Between these two extremes there are all possible intermediary forms. The shape is spherical, ovoid, lobulated or very irregular with outpouchings and fistulous tracts running in different directions.

Since the relations to the bronchi are not such as to favor a perfect drainage the cavities usually contain pus. The opening of the bronchus into the cavity is often above the fluid level; or the bronchus enters the cavity under a sharp angle; or the bronchus is twisted and kinked or its lumen is blocked by inspissated pus. The content of the cavities is thick, creamy, yellow or yellowish green or blood tinted from small hemorrhages in the limiting membrane. In some instances it is mucoid and viscid or thin and watery. Recent cavities often show pieces of softened cheesy material suspended in the pus. Erosion of an artery causes the cavity to become filled with blood clots which may arrange themselves in concentric layers (Fig. 18).

The wall of the cavities consists of several layers. On gross examination one finds the inside covered by an adherent, soft and friable yellow gray membrane which rests upon firm purple red or purple gray tissue (see Color Plate II). Microscopically the membrane on the inside is composed of necrotic tissue, degenerating leukocytes and fibrin. In this necrotic tissue the tubercle bacilli proliferate luxuriously and often form dense clumps. The lentil-shaped bodies in the sputum of patients with cavities which are so exceedingly rich in bacilli are pieces of the necrotic membrane. The membrane passes without sharp border into a granulation tissue with numerous small round cells. Towards the periphery the cells decrease in number and collagenous fibrils now are pre-

dominating (Fig. 19). Where it fuses with the adjacent lung tissue the granulation tissue again becomes more cellular. Epithelioid cell tubercles and giant cells are scanty in the wall of tuberculous cavities. The cavities of pneumonic origin usually do not show any specific changes in their limiting membrane.

In older cavities ridges protrude from the inside and trabeculae cross the lumen to fuse with opposite walls (see Color Plate III). These ridges and trabeculae

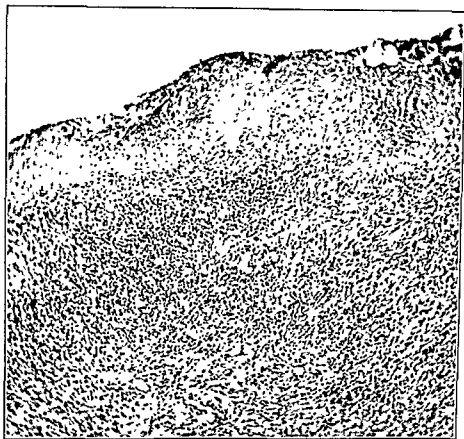


Fig. 19—Wall of a tuberculous cavity. The inside of the cavity is lined by necrotic tissue with degenerated pus cells. The necrotic tissue passes into a cellular non-specific granulation tissue. X 150

which consist of a firm, fleshy tissue are very characteristic of the tuberculous cavities. They are derived from the larger blood-vessels which resist the liquefaction. While the veins are occluded by thrombi the arteries show proliferative changes of all three layers which may terminate into the complete obliteration of the lumen. The chronic, sclerosing and obliterating panarteritis is tuberculous in nature (Laubry, Huguenin and Thomas<sup>78</sup>) and is most intensive on the side of the vessel which faces the lumen of the cavity. Because of the occlusion of the lumen of the arteries and veins the trabeculae may finally break and their free ends may be floating in the pus without causing hemorrhages. But in spite of the productive, obliterating processes an aneurism develops sometimes from an artery in a tuberculous cavity which may rupture and cause a most severe

and usually fatal hemorrhage. This aneurism formation will be taken up in the next chapter which deals with Pulmonary Hemorrhage in Tuberculosis.

The tuberculous cavities grow by progressive involvement of the capsule and by fusion with adjacent foci of suppurative liquefaction. It is this latter mechanism which causes the lobulated shape of many cavities. Since the cavitation affects chiefly the peripheral portions of the lung the visceral pleura often becomes part of the limiting membrane. The caseation and suppuration affects finally also the pleura but perforation of the cavity into the pleural sac is relatively rare because adhesions form before the pleura is destroyed. Perforation into the pleural sac, however, does occur when areas of caseous pneumonia melt down very rapidly. Points of predilection for this perforation are the lower, lateral parts of the upper lobes. Pneumothorax and pyothorax are the dangerous consequences of the perforation of a tuberculous cavity into the pleural sac.

*Sites of Aspiration Foci.*—As continuous sources of massive aspiration the tuberculous cavities cause very rapid dissemination of the infection. In order of frequency the most common sites of these aspiration foci are as follows: (1) the lateral lower angle of the upper lobes; (2) the apex of the upper lobes; (3) the periphery of the middle and lower lobes; (4) the lingula; (5) the medial part of the upper lobes above the hilus; (6) the apex of the lower lobes; (7) the base of the lower lobes (Graff and Gonnermann,<sup>79</sup> Page<sup>15</sup>). The aspiration foci are acinous-nodose, productive or exudative in nature and one finds often both types of lesions together, the exudative type being the more recent one.

According to the thickness of the capsule one can distinguish between thin walled and thick walled cavities. The thin walled cavities appear as sharply defined, spherical, punched out holes in a relatively unchanged lung tissue (see Color Plate). They are most commonly observed in connection with early infra-clavicular infiltrations and are due to the quick liquefaction of a well circumscribed area of caseous pneumonia with prompt and effective limitation. The punched out cavities give a much better prognosis than the thick walled variety, under surgical treatment they collapse easily since their thin wall does not resist the increased intrapleural pressure. Their smooth wall does not offer to the tubercle bacilli the hiding places which are found in the thick walled and lobulated cavities.

*Do tuberculous cavities heal?* This question has caused much ardent controversy and, in general, the morbid anatomists are much less optimistic than the clinicians although they admit that below a certain size cavities may obliterate. Gräff<sup>80</sup> and others give cherry size as the upper limit for healing (1½ to 2 cm.). Hart,<sup>81</sup> Hansemann<sup>82</sup> and others think that three to four cm. is the maximum diameter of a cavity that may heal. The anatomical study of the cases with long standing pneumothorax or thoracoplasty will considerably help settle these discrepancies. It is, of course, the question of what should be considered as healing. Complete restoration of normal condition does not occur, though circumfocal emphysema may obscure small scars. There are two possibilities; namely, the open healing and the closed healing. In the case of open healing the pyogenetic membrane gradually disappears and the internal lining of the cavity becomes smooth and shiny. In places, transitional or squamous



epithelium derived from the bronchi may cover the free surface. The sputum is free of tubercle bacilli and there is no immediate danger of progression or aspiration. Microscopically one finds, however, in the membrane an occasional small epitheloid cell tubercle or a small caseous area with a few tubercle bacilli. Hence, the infection is only silent and may flare up again. The cavity may also become the site of nonspecific secondary infections with abscess and gangrene formation and progressing cachexia. Another late complication of a silent tuberculous cavity is the development of a carcinoma from the islands of metaplastic epithelium. The ideal form of healing is, therefore, the closed form in which the cavity is obliterated. The closure may be brought about by collapse of the walls which touch each other and fuse together, or the cavity decreases so much in size by the shrinking of the wall that the remaining lumen can be filled by healthy granulation tissue. The result of both processes is a scar which, according to our present knowledge, is not typical and does not indicate its origin from a cavity.

Granted even that the tuberculous cavities heal more frequently than the anatomical findings suggest, the cavitation remains the most serious form of the tuberculous tissue destruction and the main cause of the phthisic death. L. and L. R. P. Barnes<sup>83</sup> followed the fate of 1454 patients in whom tuberculous cavities had been diagnosed. Eighty per cent. of these patients died within one year, 82 per cent. within 2 years and 95 per cent. within 15 years. The average duration of life of 270 patients with cavities from the appearing of the signs of cavitation was 15.8 months. Bacmeister<sup>84</sup> gives the mortality rate of people with cavities as 60 to 80 per cent and adds that the remaining patients may enjoy fair health and working capacity for many years. The great progress in the roentgenological diagnosis of incipient pulmonary tuberculosis and in the surgical treatment of cavities will undoubtedly make future statistics more favorable. As far as the roentgenological healing of cavities is concerned it should be kept in mind that focal areas of bullous emphysema which are surrounded by indurated lung tissue and which are apt to disappear spontaneously by collapse, may cast ring shadows suggestive of cavitation.

*Bronchogenic Cavities.*—So far I have been dealing with the cavities that originate from the destruction of lung tissue. Besides these pulmogenic cavities there are also bronchogenic tuberculous cavities (Borst) which are, however, of much less significance. The bronchiectatic cavities in the indurative form of pulmonary tuberculosis have already been referred to. Bronchogenic cavities may also develop from the caseous destruction of the wall of a larger bronchus or a bronchus may become involved by a progressing pulmogenic cavity. There is also the possibility that a preëxistent bronchiectatic cavity may become secondarily infected with tubercle bacilli.

#### PULMONARY HEMORRHAGES IN TUBERCULOSIS.

The most important and the most dangerous source of pulmonary hemorrhages are the *aneurisms* of the *pulmonary arteries* which develop occasionally in the wall of tuberculous cavities. These hemorrhages are sometimes so exten-

sive as to cause death from suffocation by blocking the large bronchi and the trachea. In cachectic patients the loss of blood may end the life abruptly. In many instances, the pulmonary hemorrhage is the starting point for a galloping progression of the disease. It is from the blood filled cavities that aspiration is most massive and in the soft blood clots the tubercle bacilli seem to find ideal conditions for their rapid multiplication. In addition, the loss of blood undoubtedly weakens the patient's resistance.

Considering the great frequency of tuberculous cavities *fatal* hemorrhages are relatively rare. In only from one to five per cent. of the cases with ulcerative tuberculosis are hemorrhages the immediate cause of death. In the great majority of the cases proliferative processes occlude the arteries before they are exposed to the destructive action of the tubercle bacilli (Kasper<sup>93</sup> and others). Discrepancies in the rate of occlusion and progressing caseation may, however, lead to a weakening of the wall of the artery at a time when it has still to carry the full load of the blood-pressure. Adventitia, media and, finally, internal elastic membrane are destroyed by caseation necrosis and on the slightly thickened intima a layer of blood platelets is deposited. The necrotic portion of the wall is washed away by the pus in the cavity and, under the pressure in the lumen, the thin, remaining membrane is stretched and transformed into the aneurismal sac. A slight cough is often sufficient to break this thin membrane and a stream of blood spurts into the cavity. This is the mode of aneurism formation in relatively young and rapidly growing cavities.

Douglas Powell, Bogen<sup>94</sup> and others point to the fact that aneurisms are particularly apt to develop in cavities of long standing with thick and fibrotic walls. The vessels from which these aneurisms originate are partly buried in much sclerosed scar tissue. Bogen explains, therefore, the aneurism formation on the basis of a weakening of the vessel wall by contracting scars which interfere with the nutrition of the wall. In addition, there is also an increase in the intrapulmonary arterial pressure since many vessels have been occluded or destroyed.

Pulmonary hemorrhages occur also without cavitation in patients with productive or indurative tuberculosis. Ballin and Lorenz<sup>97</sup> attribute these hemorrhages to ruptures in the rigid, unelastic lung tissue caused by coughing or irregular, deep inspiration. Page<sup>99</sup> was able to demonstrate in these cases small capillary varicosities in the wall of dilated bronchioli as probable source of the bleeding.

As additional sources of pulmonary hemorrhages in tuberculosis I mention: perifocal hemorrhagic exudation, tuberculous ulcerations in the bronchi eroding branches of the bronchial arteries or the accompanying pulmonary arteries, ulcerations in bronchiectatic cavities and, finally, the bronchial lymph node cavities, described on page A-116. In particular, this later source is easily overlooked at autopsy if one is not familiar with the aneurisms in the lymph node cavities.

### CHANGES IN THE LYMPH NODES ASSOCIATED WITH ISOLATED PULMONARY TUBERCULOSIS.

In striking contrast to the severe, massive caseation of the regional lymph nodes in the first stage of the tuberculous infection the isolated pulmonary tuberculosis affects usually the tributary lymph nodes but very little. The bacilli are apparently fixed *in situ* (Rich<sup>89</sup>). The hilus and bifurcation lymph nodes are often shrunk and indurated and deeply anthracotic. In other cases, they are moderately swollen, moist and their pigment content is diminished. The



Fig 20.—Fibrosed tubercles in a pulmonary hilus lymph node. The section is taken from a case of chronic ulcerative pulmonary tuberculosis. In addition to the fibrosed tubercles there is near the capsule a young epitheloid cell tubercle with a central giant cell. X 150

naked eye fails to detect specific changes. Microscopically there is a dilatation of the sinuses, indicating a stasis of the lymph flow and a swelling, proliferation and desquamation of the sinus endothelium (so-called sinus catarrh). The reticulum is thickened and there are focal hyaline scars (Fig 20). Epitheloid cell tubercles with giant cells are quite common. They do not tend to undergo caseation but quickly change into the hyaline scars previously mentioned. The insignificant, specific productive changes may be part of an abortive, late generalization in which single epitheloid cell tubercles are also formed in other organs (liver, spleen, kidneys). This abortive late generalization was clearly recognized

by Ranke who considered it as due to a terminal dissemination. Marked caseation of the lymph nodes is rare and is found especially in the puberty type of the isolated pulmonary tuberculosis (Aschoff<sup>90</sup>).

### PULMONARY CHANGES IN LATE GENERALIZATION.

This chapter deals with the pulmonary tuberculosis which occurs as part of a generalization of the disease in adult life. This generalization does not show an immediate connection with the primary lesion which is usually found completely healed. Its classical and best known form is the miliary tuberculosis beyond childhood. Anatomically the lesions of the different organs are of uniform size, age and nature but their density may vary. In some cases the lungs are most severely affected while in other cases the miliary dissemination is most marked in the organs of the systemic circulation.

The highest incidence of the early miliary generalization is found in the second and third year of life. The number decreases rapidly with progressing age to reach the lowest level in the second decade. The climax of the late miliary generalization occurs between the ages of 25 and 45; but single cases are observed also in very old individuals. In adults who are exposed to the tuberculous infection for the first time or in whom a true reinfection takes place, an eventual miliary tuberculosis carries the earmarks of the early generalization, that means that it is directly linked with the primary complex.

In the majority of the cases of late miliary generalization the source of the invasion of the blood stream is found in an old fibrocaseous focus, notably in a thoracic or abdominal lymph node. In some instances the generalization takes its origin from a fibrocaseous tuberculosis of the prostate, seminal vesicles, epididymis, Fallopian tube, urinary tract or adrenal or from a tuberculoma of the brain or from a tuberculosis of a joint or bone. There are cases in which a progressive isolated pulmonary tuberculosis is terminated by the miliary dissemination. At the Montefiore Hospital of New York 10 per cent. of the men and 2.8 per cent. of the women with chronic pulmonary tuberculosis succumbed to miliary tuberculosis (M. Fishberg<sup>91</sup>). In 60 cases of late miliary tuberculosis I found the following sources:

Fibrocaseous tuberculosis of the thoracic or abdominal lymph nodes or of both.....	33 cases
Fibrocaseous tuberculosis of the prostate, seminal vesicles, epididymis, kidneys, tubes or adrenals.....	12 cases
Tuberculoma of the brain .....	3 cases
Progressing pulmonary tuberculosis of the lungs.....	12 cases
(61 per cent. of the cases of pulmonary tuberculosis.)	

Several investigators, especially Huebschmann,<sup>1</sup> stress an antagonism between the miliary tuberculosis and the progressing tuberculosis of a single organ. According to Huebschmann it is this lack of progression which makes the body so highly susceptible to the bacilli. This conception is not borne out by my experience since in 20 per cent. of the cases with miliary tuberculosis an ulcerative or acinous-nodose tuberculosis of the lungs was present.

Whatever its location may be the focus of generalization shows always signs of activation. Crops of rapidly caseating tubercles appear around the fibrotic capsule or the entire focus undergoes liquefaction. The liquefied focus may break directly into a small vein and the softened content is washed away by

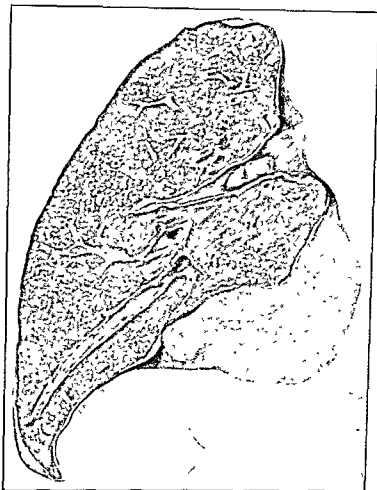


Fig 21—Intimal tubercle in the main branch of the pulmonary vein of the right lower pulmonary lobe. Late miliary generalization. Colored woman, aged 25 years. The patient was under arsphenamine treatment for secondary lues when she suddenly became ill with severe headache, stiffness of neck and vomiting. She died 20 days after the onset of these symptoms. Endoglandular tuberculous exacerbation in a lymph node at the hilus of the right lung. Diffuse miliary tuberculosis with involvement of the leptomeninges.

the blood (Loeschcke<sup>92</sup>). The liquefaction and perforation into the vessel are preceded by a local increase in number of the tubercle bacilli which often are clumped together. The form in which the tubercle bacilli enter the blood stream seems to be of considerable importance. Clumps of bacteria become more readily fixed in the finer capillaries and offer much greater resistance to destruction than single bacilli. This is borne out especially by the experimental studies of Korteveg and Loeffler.<sup>93</sup> In other cases the enrichment of the tubercle bacilli does

not take place at the point of entrance but an intimal tubercle in a larger vein becomes the source of the flooding of the blood with the bacilli. Thus, one finds for instance a solitary tuberculoma of the cortex of the brain and in a regional meningeal vein, a caseous endophlebitis. Points of predilection for the intimal tubercles are the pulmonary veins near the hilus (Fig. 21). After they have discharged their infectious content the intimal tubercles may show attempts at healing. According to my experience intimal tubercles are much more common in late generalization than they are in early generalization. There are also cases

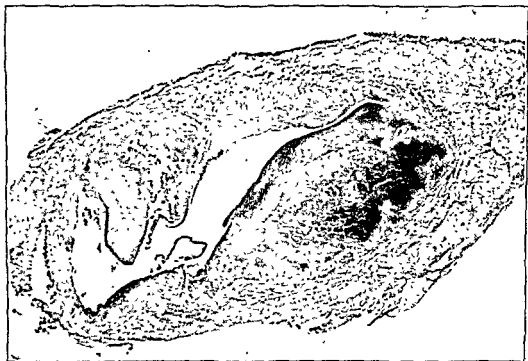


Fig 22—Caseous tuberculosis of the thoracic duct. In the wall of the duct there are two caseating tubercles. One of the tubercles is seen breaking into the lumen. The section is taken from a colored male aged 25, with a late miliary generalization. There was a caseous tuberculosis of the peripancreatic and periaortic lymph nodes. X 22.

in which the miliary generalization can be traced to a caseous tuberculosis of the cisterna chyli or of the thoracic duct secondary to a tuberculosis of the lymph nodes which drain into them (Fig. 22). In a few instances a caseated and softened lymph node may break into a large vein or into the aorta or the heart. Rich<sup>89</sup> points out that in some cases of miliary tuberculosis the lesions differ in size suggesting that they are of different age. He considers it possible that the miliary tuberculosis spreads by self-propagation. In these cases it would not be necessary to search for a source of massive invasion of the blood. At first only a few miliary tubercles are formed. They feed into the blood and lymph stream and lead to new crops of tubercles which, in turn, become the multiple centers of new dissemination.

The local proliferation of the tubercle bacilli, the flaring up of the old lesion, the softening, the formation of intimal tubercles and the rapid hematogenous

spread of the infection over the entire body are the outcome of a sudden change in the resistance of the individual. After many years of high resistance the body returns to the high susceptibility which marks the *second stage in Ranke's classification*. In some cases one is able to link this change in the resistance with extrinsic factors. I refer particularly to gestation, lactation, diabetes mellitus, leukemia and typhoid fever. In many instances, however, the cause remains obscure.

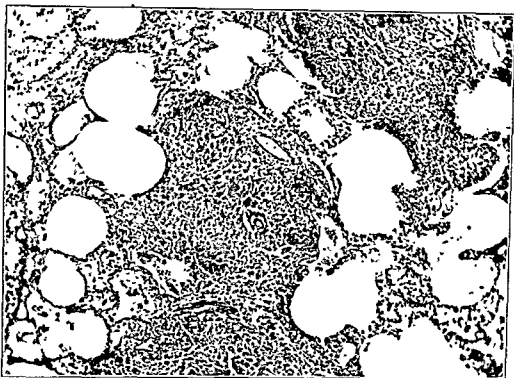


Fig 23—Productive miliary tuberculosis of the lung. The section shows several epithelioid cell tubercles with central caseation and giant cells. Note the absence of a perifocal reaction as compared with Fig 4. The section is taken from the lung of a white male aged 62 years who died from a late miliary generalization following the exacerbation of a chronic fibrocaseous tuberculosis of the prostate and epididymis. X 150.

In very rare cases of most acute miliary tuberculosis (*sepsis tuberculosa acutissima*-Loeschcke,<sup>92</sup> Tendeloo<sup>94</sup> and others) the lesions consist microscopically of necrotic tissue without defense reaction. These miliary foci of primary tissue necrosis are exceedingly rich in tubercle bacilli. They occur when the body is unable to mobilize any of its defense forces. In the cases which come to death within from two to four weeks after the onset of the dissemination the miliary nodules are essentially exudative-caseous in character. During the course of the dissemination the body may be able to regain partially its resistance and the initial exudative-caseous lesions become surrounded by a zone of specific granulation. The nodules then are less densely distributed; they are firmer, transparent and there is little perifocal reaction about them.

The quicker the restoration of the resistance the more marked are also the productive changes. In the cases of subacute miliary tuberculosis with a duration of from eight to ten weeks the epithelioid cell formation surpasses the central exudative caseation (Huebschmann,<sup>1</sup> Fig. 23). In the chronic form the lesions are loosely scattered, firm and essentially productive with the tendency to become transformed into miliary scars (nodule fibreux-Berzancon and Delarue<sup>95</sup>). It is very likely that there are cases of chronic miliary tuberculosis which ultimately heal with very little permanent damage and insignificant structural changes.

Recently considerable interest has been devoted to the protracted forms of late generalization in which the hematogenous metastases to a single organ, in particular to the lung, give rise to a progressing tuberculosis (Assmann,<sup>96</sup> Ulrici,<sup>97</sup> Schuermann,<sup>98</sup> Pagel<sup>99</sup>). This progressing hematogenous pulmonary tuberculosis is found especially in association with a tuberculosis of the bones, joints or genito-urinary tract. It has been stated by Pagel and Schuermann that this form of pulmonary tuberculosis reveals several characteristic anatomical features. Pagel describes smooth perifocal infiltrations about exudative-necrotic foci, punched out, thin walled cavities similar to those found in connection with the infraclavicular infiltrations, and productive, indurative processes which involve chiefly the marginal portions of the lobes. Schuermann calls attention to an indurating, reticular lymphangitis radiating from hematogenous foci and eventually leading to distinct clinical manifestations in form of dyspnea, cyanosis and hypertrophy of the right ventricle of the heart.

### TUBERCULOSIS OF THE PLEURA.

Tuberculosis of the pleura is always secondary. The infection usually reaches the pleura by direct extension from a focus in the lung. In some instances, the infection can be traced to a caseous tuberculosis of thoracic lymph nodes or of the chest wall. Tubercle bacilli may also be carried to the pleura by way of the lymph and blood-vessels (W. S. Miller<sup>100</sup>). Hematogenous infection is observed as part of an early generalization. Lymphatic spreading conveys the infection from the peritoneal cavity to the pleura.

Anatomically one can distinguish between exudative and productive forms of the tuberculosis of the pleura; both processes, however, often occur together (Randerath<sup>101</sup>). It is interesting that the severe forms of tuberculous pleuritis frequently present themselves under the picture of an isolated tuberculosis, the changes in the lung being insignificant as compared to those in the pleura, and often revealing distinct tendencies to heal. These observations clearly point towards the existence of a local organ immunity. This holds particularly true of the cases in which the lung is found covered by a layer of caseous material which may be several centimeters thick. The caseous material takes its origin from an exudate which at first is fibrinous in character. The trabeculae of fibrin swell up by the absorption of water and are transformed into homogeneous masses while the cellular elements of the exudate become necrotic. Later, the homogeneous masses break down to granular and fatty debris. On



each side, the caseous layer is bordered by granulation tissue which is derived from the visceral and parietal pleura and carries epithelioid cell tubercles. When the caseous exudate is not too abundant it may become completely substituted by this granulation tissue and lung and chest wall are plastered together by very dense, sclerotic membranes. Thick caseous deposits become encapsulated by the granulation tissue and undergo calcification and eventually ossification. The resulting stony plates cover the lung like a cuirasse.

In other instances the pleuritis is chiefly productive. The visceral and parietal pleura are fused together and on transverse sections one sees a purple gray or purple red granulation tissue with chains of confluent, caseating tubercles. There are also cases of a more circumscribed productive, caseous tuberculosis of the pleura with isolated, tumor-like, conglomerate tuberculomas. Combination of these productive processes with exudation leads to sero-fibrinous or hemorrhagic effusions. The pleural sac then is filled by a cloudy fluid rich in polymorphonuclear leukocytes or by a bloody fluid and the surface of the lung and the inside of the chest wall are covered by a fibrinous membrane after stripping of which yellowish gray nodules become visible. In the earliest stages the pleuritis may lack anatomic specificity, the tubercles appearing with the onset of the organization of the exudate.

The lack of anatomic and histologic specificity is particularly striking in the purely serous effusions which carry the earmarks of a massive perifocal exudation in a highly sensitive, allergic individual. The lesions in the lung often consist of an insignificant or incipient apical or subapical tuberculosis. The freshly formed serous fluid contains a moderate number of polymorphonuclear leukocytes which later give way to small round cells and desquamated mesothelial cells. In many cases tubercle bacilli can be demonstrated in the fluid *by animal inoculation or by one of the modern culture methods*; but there are also cases in which the fluid proves to be absolutely sterile. It is the high incidence of subsequent, progressive, pulmonary tuberculosis which indicates the tuberculous nature of the abacterial effusions. I believe, however, that other infections too, *e. g.*, *rheumatic fever*, may cause a purely serous effusion. *Autoptic observations on serous pleural effusions are, of course, scanty.* After removal of the clear fluid from the pleural sac one finds the pleura covered by a thin veil of fibrin underneath of which the mesothelial cells are swollen, fatty, degenerated and desquamated. The submesothelial, elastic and areolar layers of the pleura are infiltrated by leukocytes, lymphocytes and histocytes. Later, the pleura becomes thickened by newly formed connective tissue and the fibrin is organized. Tubercle formation does not take place.

The most severe form of exudative tuberculous pleuritis is the empyema. It follows the perforation of a liquefying caseous lesion of the lung or of a cold abscess into the pleural cavity. When a tuberculous cavity breaks into the pleural sac secondary invaders, especially streptococci, are often present in the pus and the rôle of these secondary infections seems to be very important.

In miliary tuberculosis of the pleura there is often no free exudate in the pleural sac since the marked distention of the lung prevents its formation.

*Pleural Adhesions.*—The pleural adhesions which are so commonly found in cases of isolated pulmonary tuberculosis result from the organization of fibrinous exudates. They may be restricted to the infiltrated portions of the lung or they may extend beyond them, often affecting the whole lung. The structure of the adhesions depends upon whether the fibrin formation was associated with a fluid exudation or not. Dry, purely fibrinous exudates lead to diffuse adhesions and the thicker the layer of fibrin the denser and firmer are the adhesions which develop. Induration of the loose connective tissue underneath the parietal pleura as part of the organization fixes the lung so firmly to the wall of the chest that it can be removed only by sharp dissection. Free fluid in the pleural cavity and especially between the trabeculae of the fibrin causes the adhesions to be circumscribed and thin, offering little resistance to separation. I believe that the fine, veil-like adhesions may disappear spontaneously under the constant strain of the respiratory movements. This accounts for the fact that indurated apices with a cartilaginous pleural cover may be found free at autopsy. Microscopically the adhesions consist of a nonspecific fibrillar connective tissue. The isolated bridges and membranes are covered by mesothelial cells.

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## CHAPTER V.

# PATHOLOGIC PHYSIOLOGY OF THE TUBERCULOUS LUNG.

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### INTRODUCTION.

The study of the diseases of any organ is based upon the careful analysis of their clinical manifestations and upon the thorough investigation of its morphologic changes and functional disturbances. Upon this tripod stands our knowledge of each particular disease. Pathology and bacteriology on the one hand and pathologic physiology on the other supplement each other in the comprehension of the etiology, pathogenesis, symptomatology, evolution and complications of the morbid syndrome; and allow one, to a great degree, to judge the prognosis and elaborate a treatment based upon scientific foundations.

It must be understood, however, that necessary as the study of histopathologic changes may be, it cannot and should not supplant or overshadow the study of functional disturbances. Meakins and Davies,<sup>30</sup> dealing with respiratory functions in disease, have justly remarked that gross structural changes may not necessarily interfere with essential functions of an organ while very slight morphologic changes may incapacitate its physiology. Moreover, a great impairment of the functions of an organ may occur without any recognizable structural changes.

**Functional Disturbances.**—If this be true of other organs it is certainly more so of the lung, which presides over the most complicated and important functions of our body, namely respiration and circulation. It is peculiar, therefore, that while in every textbook dealing with diseases of other organs (as for example the heart, kidneys or liver) the study of the pathologic physiology of the disease has been given an important place, a similar effort has not been made in textbooks dealing with tuberculosis of the lung. It seems that phthisiologists have been so thoroughly absorbed in the gross and microscopic pathology of the disease that they have lost sight of the significance of the disturbances of gas exchange, circulation, mechanics and physiochemistry occurring in the tuberculous lung, and the importance of such disturbances in the evolution of the disease. I think that paramount issues have been neglected. I shall quote for illustration in the lung following pneumothorax and more especially those following stenosis or obstruction of the bronchi, which as a rule accompanies pulmonary tuberculosis; of the effects of physical factors upon the production of cavities, and upon their evolution, persistence, increase in size and disappearance. Peculiarly enough, and notwithstanding the intensive study of the tubercle bacillus, a number of biological factors connected with the respiratory metabolism of this microbe have only recently been investigated. I

refer to its strict aërobic properties and the large amount of oxygen necessary for its life and growth. The same lack of interest has been shown in more complicated biological problems, such as anoxemia and fibrosis.

The above problems have attracted, to a greater degree, the attention of thoracic surgeons, especially those interested in pulmonary tuberculosis. Faced with unexpected and often unexplained catastrophes as well as no less paradoxical successes, thoracic surgeons have started inquiry about their causes and mechanisms. We can say, that thus far both laboratory and clinical investigations have given interesting and encouraging results which seem to lead to still untrodden paths. It is my belief that in the future more knowledge of pulmonary tuberculosis may spring from these still unexplored wells than from the thoroughly investigated morphology of the tuberculous lung. It is not impossible that this disregard of physiochemistry and pathologic physiology is, at least in part, responsible for the little progress made in our knowledge of the disease since the discovery of the tubercle bacillus by Koch in 1882; and for the obscurities, unexplained points and even unwarranted statements which have passed unchallenged from textbook to textbook.

For these reasons it has been considered timely to break with established traditions and to give a special place to the pathologic physiology of pulmonary tuberculosis in this treatise.

In the following, after a *resumé of fundamentals*, namely: *mechanics of respiration*, physiology of gas exchanges, physiochemistry of  $O_2$  and  $CO_2$ , mechanism of gas absorption in the lung and the pleura, regulation of respiration and the respiratory metabolism of the tubercle bacillus, the phenomena due to the disturbances of these functions caused by pulmonary tuberculosis will be studied. These are, phenomena due to disturbance of pulmonary ventilation and circulation by mechanical causes, such as bronchiostenosis and bronchial obstruction, pneumothorax, phrenicectomy and thoracoplasty; the mechanism and pathologic physiology of the production and further evolution of tuberculous cavities; and, in conclusion, the mechanism of cure of tuberculosis by rest or surgical collapse treatment.

## I. MECHANICS OF RESPIRATION.

(a) **Respiratory Movements of the Chest.**—Normal breathing is accomplished by rhythmic movements of expansion and contraction of the chest, (brought about by the movements of the ribs, the sternum and the diaphragm) so that the capacity of the chest alternately increases and decreases.

The lungs are suspended by the trachea in an air-tight cavity; these organs are covered on all their surfaces by the pleural membrane, which is reflected from the hilum of the lung towards the walls of the chest. The apposition of the reflected pleural membranes in the median and the anteroposterior planes forms the mediastinal septum. The pleural layer covering the lungs is the splanchnic pleura and the layer covering the chest walls is the parietal pleura. The latter is attached to the endothoracic fascia from which it can be easily stripped, as is done in extrapleural pneumolysis.

Under normal conditions the two pleural layers, parietal and splanchnic, are in complete contact so that there is no real pleural cavity. Even if air is artificially introduced into the cavity, it will be gradually absorbed. The mechanism is the same as that which causes the absorption of air in the lung following obstruction of a bronchus or of air injected into the peritoneal cavity or the subcutaneous tissues. This mechanism will be explained later.

In the fetus, before respiration, the lungs do not contain air; the fetal lung is atelectatic or better "apneumatic"; its specific gravity is slightly greater than one ( $\approx 1.05$ ) so that it sinks in water. For the same reason its volume in cubic centimeters is slightly less than its weight expressed in grams. The importance of these facts will be shown when atelectasis is studied. In the fetal period of life the lungs completely fill the chest; a needle introduced into the pleural cavity shows that the pressure in it is atmospheric. Thus in the fetus there is no "negative" pleural pressure.

After the first respiratory movement the mechanics of the chest change radically. The capacity of the chest cavity is increased so that the lungs must follow and become distended; for when the chest is expanded the intrapulmonary pressure is decreased and air rushes through the trachea into the lungs. From this time, until the adult period is reached, the chest develops more rapidly than the lungs, leading to a disproportion between the capacity of the chest and the volume of the lungs. The lung, being a perfectly elastic organ, stretches so that it fills completely and constantly all the free space in the chest. However, in doing so it exerts a pull on the visceral pleura and tends to separate it from the parietal pleura; this "pulling of the stretched lung," due to its elastic recoil, is the cause of the "negative pressure" in the pleural cavity, which is, as could be foreseen, equal to and varies with the elastic recoil of the stretched lung. Therefore, it is greatest at the end of inspiration when the stretch of the lung is at its maximum and smallest at the end of expiration; the conception that the "cohesion" between the two layers of the pleura is of great importance does not seem justified. From the above it is evident that expansion of the lung on inspiration is due to and follows the increase of the chest capacity and, conversely, that its expiratory collapse is due to the return of the chest to its normal position. Air rushes into the lung because the lung expands rather than that the lung expands because air enters it, as is often believed. Thus the normal position of the lung is in collapse, which state the lung will assume whenever it is not obliged to do otherwise. In fact, when air is introduced into the pleural space so that the pressure in it becomes less negative, the lungs will expand only partially. If the pressure becomes atmospheric, as when the chest wall is widely opened, the lung will remain collapsed.

The inspiratory enlargement of the chest is brought about by the elevation of the ribs and the contraction of the diaphragm. When the ribs are pulled upwards by the respiratory muscles, they tend to become horizontal as their anterior extremities and the sternum are elevated from an obliquely downward position. By this bucket-handle movement both diameters of the chest, anteroposterior and lateral, are increased. The contraction of the diaphragm, during which its curvature is flattened, produces an enlargement of the vertical axis. Further

more, the diaphragm, with its fulcrum on the abdominal viscera, brings the costal borders outwards, thus further enlarging the base of the chest. When the relaxed inspiratory muscles and the diaphragm resume their normal position of rest, a portion of the air contained in the lungs, directly proportionate to the decrease of the chest capacity, is expelled.

*Elevator Muscles*.—It is evident that all the elevator muscles of the ribs are inspiratory; they are: the external intercostals, the pectorals, the rhomboid and trapezius, the serrati and the scaleni. Expiration, on the contrary, being mostly a passive phenomenon, hardly needs muscular contraction. It should be remembered, however, that the inspiratory muscles tend to control the dropping of the chest during expiration and render easier the start of the next inspiration. In conditions which produce a marked decrease of muscular tonus (such as shock, anoxemia with acapnia, or paralysis of these muscles as in poliomyelitis) the capacity of the chest and its inspiratory expansion are greatly decreased. This point is of great importance in shock, especially after thoracoplasties because it further increases the always present anoxemia in these cases.

*Abdominal Muscles*.—The abdominal muscles take an active part in forced expiration. Their active contraction at the end of expiration not only pulls the lower ribs and the sternum downwards but also pushes upwards the diaphragm by exerting pressure on the abdominal viscera. Their action is of special importance in the production of cough. In cases of marked weakness of the abdominal muscles and splanchnoptosis the diaphragm is thrown out of action.

The physiology of the diaphragm must be considered more especially in its relation to the production of cough and to the changes produced in respiration by its paralysis following phrenicectomy.

(b) *Diaphragm.—Mechanism of Cough*.—Cough is a reflex induced by irritation of the tracheobronchial or laryngeal mucosa; it is composed of two separate and distinct acts that is, a deep inspiration followed by a violent expiration. In the expiratory act I think that two separate phases should be distinguished. The first is of short duration; during it the glottis remains closed while the expiratory muscles contract and thus raise the pressure of the air in the lung. This I shall designate as the "compressive phase." In the second the glottis is slightly opened while expiration goes on so that a violent draft of air is produced, tending to expel any material present in the bronchi. This is the "expulsive phase." In other words, cough can be compared to the three phases of the explosion of a cartridge in a gun. The inspiratory act corresponds to the loading of the gun, the compressive phase to the combustion of the powder and the expulsive phase to the projection of the bullet from the mouth of the barrel.

The diaphragm being a purely inspiratory muscle takes an active part only in the inspiratory phase of cough. After a deep inspiration, the glottis closes while the diaphragm remains contracted thus adding to the immobilization of the thorax; in the following prolonged expiratory effort the chief part is played by the abdominal muscles, which contract forcibly, exerting pressure on the viscera, which in turn push the diaphragm upwards, thus increasing the in-



trathoracic and intrapulmonary pressures. The diaphragm takes only a small part in the expiratory phase. And, contrary to the general opinion, I believe that its action is directed against the action of the abdominal muscles. In fact, by its contraction it limits and controls the visceral push, and in that way regulates the expulsive force of the cough. It is precisely the elimination of this function of control which is responsible for some of the puzzling phenomena observed following phrenicectomy.

When a sufficient positive pressure is reached, 60 to 80 mm. Hg, the glottis opens slightly, while the abdominal muscles and the expiratory muscles (the internal intercostal and serratus posticus inferior) continue to contract and thus tend to keep the pressure constant. Under the fluoroscope we clearly see that during cough the diaphragm is pushed "upwards," which shows that it takes no active part in the cough process, since contraction of the muscle would produce a lowering of the diaphragm.

More recent experimental investigation (Oppenheimer,<sup>39</sup> Hare and Martin,<sup>13</sup> Lemon,<sup>28</sup> Coryllos and Birnbaum<sup>9</sup>) and clinical data of a considerable number of bilateral phrenicectomies published to this date (Neuhofer,<sup>38</sup> Sauerbruch,<sup>46</sup> Lange,<sup>27</sup> Ghose,<sup>10</sup> Dowman,<sup>8</sup> Iselin,<sup>14</sup> Pickhardt<sup>45</sup>) have modified our concepts of the physiology of the diaphragm and of its importance in respiration. It is at present considered that the diaphragm serves principally to maintain the vertical diameter of the chest. Unilateral or even bilateral paralysis of the diaphragm, produced by temporary blocking or even by avulsion of one or both phrenic nerves, does not interfere with the movements of the lung in respiration. Even when slight temporary dyspnea was noted following bilateral phrenicectomies it always cleared up very rapidly. A child upon whom Sauerbruch<sup>46</sup> had performed a bilateral phrenicectomy had a normal vital capacity three years later and engaged in gymnastics although both diaphragms were elevated and immobile. The same applied to six bilateral cases of Curti,<sup>7</sup> Cardis and Malinski,<sup>2</sup> Jehn<sup>22</sup> and others. These newer conceptions of the importance of the diaphragm as a respiratory muscle should be taken into consideration in our appreciation of the results obtained by phrenicectomies in pulmonary tuberculosis. Personally I believe that the mechanism of closure of cavities by phrenic interruption, which can occur and has been reported in a small number of real cavities, is not to be found in the supposed "relaxation" or compression of the diseased lung,\* but in the collapse or kinking of the bronchial outlet of the cavity, which may sometimes occur even with incomplete pneumothorax. This point will be developed later.

(c) **Respiratory Movements of the Lung.**—At the outset we must admit with Macklin<sup>30,36</sup> that "lung is the bronchial tree with the complex of peripheral twigs and leaves of the tree closely dovetailed with their connective tissues, blood, lymph nodes and nerves." The physiological respiratory unit is the alveolar duct system enveloped by numerous and thin-walled out-pocketings, the alveolar sacs and simple alveoli (Miller,<sup>37</sup> Wilson,<sup>51</sup> Lagasse), which arise

\* It is an open question whether paralysis of the diaphragm immobilizes the corresponding lung. In a recent paper on Roentgen Kymography in Phthysiology, Bernard, *et al.*, have shown that the diaphragm moves as much as before but in the opposite direction. (*Presse Méd.*, 2: 2053, 1933.)

from fine uniloculated terminal respiratory bronchioles. These bronchioles, partly conducting and partly respiratory, are enabled to enlarge and diminish in size by the elastic meshes and the smooth muscular fibers which encircle them. Their diameter is smaller than that of a fine sewing needle (Keith<sup>24, 25</sup>). They run into larger bronchi and so on until all the bronchi of a lobe merge into a lobar bronchus; the lobar bronchi in turn merge into the respective common bronchus and finally into the trachea. It is thus possible to distinguish in the lung: (1) the central system, formed by the purely conducting bronchial tree, and (2) the peripheral system, partly conducting and partly respiratory, represented by the respiratory bronchioli, lobules, acini and air sacs. Both systems constitute a continuous functional entity, so that in respiration air passes from the larger to the smaller branches and, through the terminal bronchioles, ebbs and flows into and out of the lobules (Macklin<sup>34</sup>). It is obvious that adequate respiration requires the patency of the respiratory tubes, the integrity of the respiratory membrane, the synergetic action of striated and smooth muscles, and the normalcy of pulmonary circulation.

*The Bronchi.*—The bronchi during inspiration present marked changes both in their diameter (Jackson,<sup>10</sup> Heinbecker,<sup>14</sup> Francis<sup>9</sup>) and in their length (Macklin,<sup>34</sup> Hudson<sup>16</sup>). The anatomical construction of the whole tree from the trachea to the finest bronchioles is adapted to these changes. During inspiration their diameter and their length increase under the action of the expanding chest and of the negative intrapleural pressure. During expiration both diameter and length decrease, due to the action of the elastic membrane of the bronchial tree (Macklin<sup>30</sup>) which extends continuously in the tunica propria from the larynx to the small bronchi, and to the active contraction of the bronchial muscles, as will be shown later. These movements are well shown in Fig. 1, borrowed from Macklin. It is interesting to note that because of the negative intrapleural pressure the bronchi can increase in diameter and length at the same time, which would be impossible if the intrapleural pressure did not become more negative as inspiration progressed. "It is apparent," says Macklin,<sup>34</sup> "that when the bronchial tree elongates or shortens, all the structures which duplicate its ramifications, attached to it as they are, must do likewise. The vascular tree, representing the pulmonary and bronchial arteries and veins lengthens and enlarges synchronously with the bronchial tree to the same degree and by the same mechanism, and conversely, they shorten and narrow during expiration."

This mechanism of the movements of the bronchial tree gives a satisfactory explanation of the aëration of portions of the lung which correspond to parts of the chest which expand very little during inspiration; an accurate knowledge of these details is of great interest to phthisiologists.

*Expansion.*—Keith<sup>24</sup> (1909) has shown that expansion in the chest cavity is lopsided and lacking in symmetry. Whereas there is considerable expansion in the bases and anterolaterally, there is very little in the posterolateral and superior portions of the chest, and scarcely any towards the costo-vertebro-mediastinal region. This "paravertebral" portion of the lung can only be aërated by a downward and forward movement of the root region of the lung. It thus becomes obvious that ventilation of this under-privileged region of the

lung (designated by Macklin<sup>21</sup> superoretro-radicular, and including the apex, a considerable portion of the upper lobes and the upper part of the lower lobes) can only be accomplished by a "circling twist of the root" produced by the inspiratory inward (median) and forward sweep of the whole lung, and only partly by an inspiratory direct traction of the diaphragm upon the heart through the phrenocardiac ligament, as suggested by Keith.<sup>24</sup>

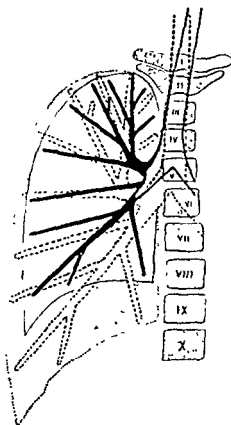


Fig. 1—Inspiratory and expiratory bronchial movements. Solid black represents bronchi in full expiration, dotted outlines bronchi in full inspiration. The outlines were copied from x-ray pictures of the thorax of the same person taken in exactly the same position, one immediately succeeding the other. (Macklin.)

This point is of great importance because it explains the predilection of tuberculous lesions and cavities for this supero-radicular segment of the lung. In fact, if Krause<sup>25</sup> and Tendeloo<sup>48</sup> are right "that bacilli lodge and create tubercles where movements, air and lymph flow are least," then it becomes clear that any cause which would interfere with free movements of the root of the lung would impair the movements of this portion of the lung, and hence facilitate the development of tuberculous lesions in it. The multiple causes of inflammatory enlargement of the intertracheo-bronchial and bronchopulmonary lymph nodes and the ensuing anchoring of the hilum may explain the preferential localizations of superinfections in the apex, whereas primary infects are found everywhere and more often in the lower lobes. Expulsion of the air content of the lower lobes

into the apical portions during cough, as shown by the "lightening" of the apices in fluoroscopic examination, may be an additional cause. Thus, an accumulation of bacilli occurs in the upper part of the lung increasing the "dosage" of infection for that localization. Furthermore it has been shown that in quiet breathing we use only one-tenth to one-twentieth (Zuntz<sup>22</sup>) of our lung parenchyma. In fact, Zuntz has shown that the respiratory surface of the human lung is 90 square meters or 1000 square feet; if this entire surface was used for gas exchanges about 6000 c.c. of oxygen should diffuse per minute per kgm. of body weight, instead of 300 c.c. which actually pass during quiet breathing. This, however, does not mean that all the alveoli are simultaneously distended to one-twentieth of their capacity; the lung does not expand during inspiration like myriads of small elastic balloons connected by means of fine elastic tubes to a central pipe. Keith<sup>24</sup> has shown that the lung opens up like a Japanese fan, so that a number of alveoli may be more or less fully expanded while others are very little or not at all.

Now if we connect these facts with what will be shown later, namely, that the degree of ventilation in a portion of the lung is proportionate to the degree of expansion of the alveoli, to the degree of dilation and elongation of their bronchi, and to the blood flow through the alveolar capillaries, we arrive at the conclusion that all causes producing a decrease or increase in ventilation will affect the remaining factors in a corresponding way.

*Posture*—These factors should be especially borne in mind when we consider the influence of posture upon the mechanics of respiration. Haldane, Meakins and Priestley<sup>12</sup> have shown that in the recumbent position respiration is much less efficient than in the upright, and it affects the abdominal and diaphragmatic respiration; this being probably due to the compression exerted by the abdominal viscera upon the diaphragm. On the other hand, as the movements of the thorax depend upon the motility of the costal joints and especially of the sternocostal cartilages, it is easily understood that any limitation on the movements of the latter will interfere with the respiratory expansion of the chest. These facts explain the limitations of respiration in the recumbent position, and more particularly when weights have been placed upon the chest. It is obvious that under these conditions a great number of small or middle size bronchi may be unable to expand during inspiration, especially if they are narrowed because of pathological changes; they therefore remain collapsed, producing a more or less marked airlessness in the corresponding areas of the lung parenchyma. This condition can be transformed into atelectasis if these bronchi become completely obstructed for some length of time, either by edema of their mucosa, by mucus or by productive changes in their walls; on the other hand it may give rise to obstructive emphysema if during inspiration air can pass through the narrowed slightly expanding bronchi but it remains entrapped in the acini during expiration because of the expiratory occlusion of these bronchi. We shall see later the importance recently attributed to this phenomenon in relation to the cure of pulmonary tuberculosis by rest and collapse therapy (Coryllos<sup>4, 5</sup>).

(d) *Mediastinum*.—The mediastinum is embryologically homologous to the mesenterium; it extends from the posterior surface of the sternum to the ver-

tebral column. It is formed by the two mediastinal parietal pleural layers reflected around the pedicles of the lungs. Between the two layers we find the trachea and esophagus, with the vena cava superior and the arch of the azygos vein against the right pleura, while the aorta and its arch, with the big arterial vessels arising from it, are against the left pleura. Behind the sternum is the thymus gland or its remnant and numerous lymphatics, and lower down the heart covered by the pericardium. Thus the mediastinum is really a space and not a mere membrane like the mesenterium. It presents, however, two "weak points" where the two pleural layers directly meet; one behind the upper part of the sternum and the other behind the heart. These are the regions, especially the first, through which mediastinal herniæ are formed during pneumothorax. An excellent description of these herniæ has been given by E. Packard.<sup>40</sup>

The mediastinum is in some animals extremely mobile and flimsy, especially in the dog where it forms a partition readily permeable to gases and even to fluids; in the human, however, it represents a real physiological partition not permeable to gases. In children it is very mobile, while it is more rigid in adults. This steadiness, however, varies to a considerable degree according to the individuals and it is of great importance in the mechanics of the chest cavity, especially in pathological conditions of the lungs, in disturbances of the intrapleural pressures, and in pneumothorax.

When a lobe of a lung and especially when a whole lung decreases in volume, as following atelectasis and fibrosis, the intrapleural pressure becomes more negative. The mediastinum, therefore, is displaced toward the affected side, the diaphragm rises, and the healthy lung becomes more distended and often emphysematous.

In *pneumothorax*, on the contrary, as the intrapleural pressure approaches atmospheric pressure, the lung collapses, the diaphragm drops, and the mediastinum is displaced towards the opposite side. The reason for this is that the pressure in the healthy chest and in the abdominal cavity remains the same, whereas in the pneumothorax side it has increased. This phenomenon will be present even when the pressure in the pneumothorax side remains negative, provided that it is less negative than in the other side. Naturally it will be more marked when pressure becomes positive, as in tense pneumothorax.

When pneumothorax is present on one side the respiration of the contralateral lung is greatly influenced by the degree of mobility of the mediastinum. Unchanged when the mediastinum is rigid, it will be impaired in proportion to its motility and to the differences in pressures between the two pleural cavities. In fact, during inspiration, the mediastinum will tend to be "sucked" into the healthy side, as the intrapleural pressure on the unaffected side becomes more negative than that on the pneumothorax side, thus interfering with expansion of the lung; whereas, on expiration, the opposite effect will be produced, interfering with expiration to a degree varying with the pressure in the pneumothorax side. This will be further studied with intrapleural pressures (p. A-183).

*Mediastinal Emphysema.*—When air penetrates between the two layers of the mediastinum, mediastinal emphysema is produced. The result is that pressure in the mediastinum which is normally  $-4$  mm. Hg. (Assman) may be trans-

tormed into a positive pressure. These changes in mediastinal pressure have lately been carefully studied, both clinically and experimentally (Ballon and Francis,<sup>1</sup> Jessup,<sup>23</sup> Rehn<sup>44</sup>), especially in their relation to the ensuing respiratory and circulatory disturbances. This question is of importance to the phthisiologists because a considerable number of cases of mediastinal emphysema have been reported as complicating artificial or spontaneous pneumothorax. In a small number of cases they were due to injury of the lung by the needle (Sercer and Peicic,<sup>47</sup> Parfaict and Crombie<sup>41</sup>), causing air to pass between the lung and the visceral pleura to the region of the hilum and thence to the mediastinum. It is not exceptional for slight mediastinal emphysema to follow avulsion of the phrenic nerve, especially in patients with artificial pneumothorax.

Jehn and Nissen have shown that there are no noticeable functional changes until intramediastinal pressure reaches zero. After that clinical symptoms appear and progress rapidly, due to compression of the cava and pulmonary veins, decrease of the blood flow into the left auricle, a drop in arterial and rise in venous blood-pressure, leading to anoxemia and shallow breathing, cyanosis and even asphyxial death. However, because of the considerable absorbing power of the mediastinum, cures have been reported even in cases in which the pressure rose from  $-4$  to  $+35$  mm. of water.

(e) **Elasticity and Contractility of the Lung. Action of Bronchial Muscles.**—Without entering into the details of the innervation of the lung and the specific action of the vagal and sympathetic fibers which compose the pulmonary plexus, upon the vessels, glands and muscles of the lung, it is of interest to mention the more recent conceptions of the rôle of the smooth bronchial muscles.

The richness of the muscular element in the bronchi, its structural arrangement and disposition from the larynx to the alveoli, the embryological homology of the bronchi and the intestinal tract, the motility of the bronchi and the contraction of the bronchial lumina synchronous with expiration, as seen through the bronchoscope, have long since suggested the functional importance of these muscles.

Although fluoroscopic examination and radiographic investigation have shown that some kind of peristaltic movement could be elicited in the bronchi (Reinberg<sup>45</sup>), it has not been possible, thus far, to demonstrate in a conclusive way any active participation of these muscles in the respiratory movements, and even less to prove rhythmic contraction in relation to the rhythmic contraction of the striated respiratory muscles. Shortening and narrowing of the bronchi during expiration has been considered as a passive phenomenon due to the expiratory collapse of the chest and of the lung, conditioned by the elasticity of the lung.

In order to explain a number of puzzling phenomena occurring in acute or chronic pulmonary diseases, and more especially in pneumothorax, several authors have elaborated upon the elasticity of the lung. They have suggested, for example, that in lobar pneumonia the elasticity is increased (Van Allen and Wu<sup>50</sup>); they have made a distinction between an elasticity of extension (elasticity of structure) and an elasticity of expansion (elasticity of function) (Parodi); others have divided the elasticity of the lung tissue into an expansile

and contractile elasticity, and contended that pathology in the lung "may attenuate, injure or destroy entirely either the expansile alone, the contractile alone or both of them simultaneously" (Bendove<sup>2</sup>).

None of these theories can be accepted. Mechanically, when an external force, acting upon an elastic solid body, is released, this body, if perfectly elastic, will return to its initial size and shape. During expansion its potential elastic recoil increases in proportion to the force exerted upon it, and this elastic recoil represents its force of retraction, which is necessarily equal to the force which has caused its extension. Whatever may be the stretch of an elastic body under the action of forces exerted upon it, so long as its elasticity is not overstepped or destroyed (in which case we are no longer dealing with an "elastic body") the forces of extension and retraction must remain equal and opposite, so that their algebraic sum equals zero. It is impossible to conceive a change in one of these forces without an equal change in the other and, even less, the disappearance of one with persistence of the other, so long as the body remains "elastic." Temporary or permanent distention of the lung as in functional or organic emphysema and temporary or permanent contraction as in atelectasis or fibrosis, does not mean selective changes of one kind of elasticity, in the "contractile elasticity" in the first and "the expansile elasticity" in the second, as Bendove stated. It simply means a loss of elasticity and a permanent deformity as it occurs in fibrosis or emphysema or only temporary changes in shape caused by the action of external forces; in the latter case, with the removal of the causative force these changes disappear, as in atelectasis or in allergic asthma.

The theories enumerated above had been advanced because in a number of pathological conditions the lung does not behave as it should if it were a perfectly elastic organ. In atelectasis or in lobar pneumonia it is retracted and remains retracted although the intrapleural pressure has decreased (become more negative). On the contrary, in emphysema and even more in allergic asthma, it remains distended, causing an increase of the intrapleural pressure (less negative). In both instances the lung does not seem to act as an elastic organ. However, a more careful analysis of these cases shows that these apparently paradoxical phenomena are due to the interference of other factors, which have not been sufficiently considered in the above cited interpretation of these phenomena. Factors such as bronchial obstruction in atelectasis, or contraction of the smooth musculature of the bronchi in asthma, have often been neglected or underestimated.

It is true that thus far we have had no accurate knowledge of the action or of the mode of response to nervous stimulation of the smooth bronchoalveolar fibers. Only lately a more precise physiological method has been elaborated (Luisada<sup>29</sup>) which has rendered possible a more accurate investigation of the mode of contraction of these muscles and of the relation of their contraction to the respiratory movements.

**Broncho-electrograms.**—Luisada<sup>29</sup> has been able, in using a special technic, to obtain broncho-electrograms by means of the string galvanometer, in living animals and even in the human. For that purpose he uses in the human two leads, one intrabronchial and the other applied to the neck. The disturbing

electrocardiogram is eliminated almost completely from the graph by the interposition between the leads and the galvanometer of a special electro-ionic valve and an amplifier.

This new method has already given very interesting information. It has shown that the bronchial muscles of the normal individual present a rhythmic contraction and relaxation synchronous with the respiratory movements; furthermore, that contraction begins at the end of expiration and terminates just before the beginning of inspiration. The action of a number of drugs was investigated—morphine, atropine, adrenalin, histamine and others, as were also the changes occurring in the contraction of these muscles during anaphylactic shock, where a dissociation of their rhythm and the rhythm of thoracic movements constantly occurred.

*Results.*—It is still too early to judge this method and the importance of the results obtained thereby. It points, however, to the physiological importance of the musculature of the lung; it is even probable that we may have to modify our ideas upon the activity or passivity of the different phases of respiration. In fact, if inspiration is an active phenomenon and expiration a passive one so far as the chest is concerned, it seems that expiration becomes an active phenomenon so far as the lung is concerned by the active expulsion of air due to the contraction of bronchi. We do not as yet know what specific action the vagal and the sympathetic fibers have upon these muscles; or whether the latter fibers play the rôle of inhibitors of the former as they do in the intestinal muscles. Other points still to be determined are the influence of anoxemia, accumulation of  $\text{CO}_2$  and especially of inflammation upon the action of these muscles. At any rate, it appears that in the future their part in the physiological action of the lungs as organs of gas exchange should be taken into serious consideration.

## II. PHYSIOLOGY.

(a) *Gas Exchanges in the Lung.*—During inspiration and expiration about 500 c.c. of air are drawn in and out of the lungs, constituting the tidal air. On the deepest inspiration 1500 to 2500 c.c. or more can be introduced into the lung (complemental air). During the deepest expiration an amount of air varying in different individuals between 600 to 1200 c.c. remains in the lungs (residual air). This air cannot be expelled since the lung cannot collapse completely because of the difference in size between the volume of the lung and the capacity of the chest, and because of expiratory collapse of the small bronchioli and contraction of the bronchial muscles which cause the entrapping of this air in the alveoli.

*Dead Space.*—Of the air contained in the lungs a part fills the so-called "dead space," which is composed of the conductive portion of the bronchial tree in which no gas exchange takes place. The capacity of this space averages, at quiet breathing, 150 c.c. Contrary to the opinion of Krogh and Lindhard,<sup>103</sup> the capacity of the dead space is not fixed; it increases considerably, three or four times, during hyperpnea (Douglas and Haldane,<sup>75</sup> Y. Henderson, Chillingworth and Whitney<sup>93</sup>) because of the inspiratory dilation and elongation of the bronchi (Macklin<sup>100</sup>). In tuberculosis where considerable portions of the diseased and



cavitated lung may become incapacitated for gas exchanges, the dead space may become even greater. It is easy to understand that if, in a healthy individual, only two-thirds of the tidal air penetrate the respiratory portion of the lung, in a tuberculous patient this amount may be considerably less. This may result in insufficient oxygenation of the blood and retention of  $\text{CO}_2$  causing hyperpnea, which further increases the dead space and may lead to acapnia combined with anoxemia, as we shall see later.

*Gas Diffusion.*—In the alveoli the air is separated from the blood circulating in the perialveolar capillaries by the so-called respiratory membrane, composed of the alveolar epithelium and the capillary endothelium. This partition acts in the diffusion of gases as a wet membrane, the thickness of which does not exceed the diameter of a red cell. Through this membrane the gases of the alveolar air and the gases in solution in the blood diffuse from one medium to the other according to their partial pressures (Dalton), their speeds of diffusion, their coefficients of solubility, and the temperature of the media in which they are held.

Lack of space does not allow me to enter into the details of the physiochemistry of respiration. Suffice to say that the most important factor in gas exchange is the difference in partial pressures of the gases on either side of the respiratory membrane. As Paul Bert<sup>55</sup> has shown, the important factor in gas exchange is not the percentage of each gas in a mixture of gases but its partial pressure, so that each gas acts as if it were alone under pressure.

What is partial pressure? The atmospheric air is composed of 20.94 per cent. of  $\text{O}_2$ , 0.03 per cent. of  $\text{CO}_2$ , 79 per cent. of nitrogen, a variable amount of water vapor and traces of neon and argon. At sea level with an average barometric pressure of 760 mm. Hg. the partial pressure of oxygen will be  $\frac{20.94}{100} \times 760 = 159$  mm. Hg.; of carbon dioxide  $= \frac{0.03}{100} \times 760 = 0.2$  mm. Hg. and of nitrogen  $\frac{79}{100} \times 760 = 600$  mm. Hg.

In the alveolar air, because of the activity of gas exchanges in the lung, the percentages of the same gases are: oxygen 15 per cent., carbon dioxide 5 per cent. and nitrogen 80 per cent. (14.5 per cent. of  $\text{O}_2$ , 5.6 per cent. of  $\text{CO}_2$  according to Haldane<sup>55</sup>), plus water vapor to saturation. The corresponding partial pressures of these gases are:  $\text{O}_2$  130 mm. Hg. and  $\text{CO}_2$  40 mm. Hg. In the venous blood the percentages of these gases are again different because of the gas exchange in the tissues; they are:  $\text{O}_2$  5.3 per cent. (40.2 mm. Hg.) and  $\text{CO}_2$  6.0 per cent. (45.6 mm. Hg.). The corresponding volumes of these gases are indicated in the following table (Starling):

IN 100 VOLUMES OF BLOOD:

	Oxygen	Carbon Dioxide.	Nitrogen.
Arterial blood .....	20 vols.	40 vols.	1 to 2 vols.
Venous blood .....	8 to 12	51 vols.	1 to 2 vols.

The great difference in the volumes of oxygen and carbon dioxide dissolved as compared to the volumes of nitrogen is due to the fact that nitrogen is an indifferent gas and is dissolved in the blood according to its coefficient of solubility whereas  $\text{O}_2$  and  $\text{CO}_2$  enter in chemical combination; the first with

hemoglobin forming an unstable product, oxyhemoglobin, and the  $\text{CO}_2$  with alkali contained in the blood forming bicarbonates. Almost all of the oxygen in the blood is combined with hemoglobin and is contained in the red cells. In the plasma we find in physical solution only a small amount of oxygen, equal to 0.36 c.c. per 100 c.c. of blood; this amount which represents the  $\text{O}_2$  directly available to the tissues is maintained constant; as  $\text{O}_2$  is absorbed by the tissues and its tension decreases, the oxyhemoglobin dissociates and liberates the amount of oxygen necessary to maintain the oxygen in solution always at the same level.

Because of these differences in partial pressures of  $\text{O}_2$  and  $\text{CO}_2$  between the alveolar air and the venous blood,  $\text{O}_2$  diffuses from the first to the second, and  $\text{CO}_2$  in the opposite direction. The tension of these gases in the blood is the principal regulator of respiration, so that these tensions should and normally do remain strikingly constant, this being especially true for  $\text{CO}_2$ .

It must not be thought, however, that these exchanges, carried on so smoothly under normal conditions, represent small forces. In reality their activity when studied closely proves to be tremendous. The following data will give a fair idea of the forces involved and will afford us a better comprehension of their pathological physiology. The blood is in the pulmonary capillaries only about one second and yet oxygen diffuses into the venous blood fast enough to oxygenate it to arterial blood in the first two-fifths of this time. There is a variation among individuals, but a 60 per cent. margin of safety in diffusion time is always present. In small animals, such as the canary, the speed of diffusion represents a small fraction of a second, as the heart beats 700 to 800 per minute at rest (Buchanan<sup>6</sup>). This margin of safety alone is adequate to insure the complete oxygenation of venous blood should it enter the lungs entirely reduced instead of 75 per cent. oxygenated as is normal (Greene<sup>83</sup>).

It was said above that the important factors for adequate oxygenation of the blood were not the percentages of  $\text{O}_2$  and  $\text{CO}_2$  in the alveolar air but their partial pressures. In fact, if, the percentages remaining constant, the barometric pressure changes, the partial pressure will change in the same direction; so that at 29,000 feet above sea level, where the barometric pressure is reduced to 248 mm. Hg. as reported by Glasher (Haldane<sup>85</sup>) during his ascent in balloon, the partial pressure of  $\text{O}_2$  drops to 28 mm., which physiologically corresponds to 7 per cent. at sea level pressure, although the percentages of it in the air remain 20.94 per cent. This amount can hardly maintain life. Conversely, at 165 feet under the surface of the sea where the pressure is equal to five atmospheres, a 2 per cent. content of  $\text{CO}_2$  in the air breathed, which would be harmless at normal atmospheric pressure, is increased to 10 per cent., which produces severe hyperpnea and narcosis.

Outside of these extreme variations in pressure, the amounts of oxygen and more especially of  $\text{CO}_2$  contained in the blood show a striking constancy. The mechanism of this sustained equilibrium, which is of greatest importance for the comprehension of the whole question of respiration, and more especially of its regulation, is explained by the mechanism of dissociation of oxyhemoglobin and by the interaction of oxygen and carbon dioxide.

(b) **Dissociation of Oxyhemoglobin.**—Bohr, Hasselbach and Krogh<sup>50</sup> have shown (1904) that the dissociation curve of oxyhemoglobin presents a double characteristic bend (Fig. 2). Almost vertical in its initial portion, it becomes nearly horizontal at its terminal portion. As the amount of  $O_2$  in the alveolar air rises from 0 per cent. to 8.5 per cent. (60 mm. Hg.) hemoglobin absorbs oxygen very rapidly, so that its saturation rises from 0 to 90 per cent. From there on, further increase of oxygen will increase the amount of oxyhemoglobin very slowly, so that from 8.5 per cent. to 17 per cent. of oxygen (120 mm. Hg.), oxyhemoglobin increases from 90 per cent. to only 95 per cent. Conversely, in the peripheral respiration, as the oxygen dissolved in the plasma

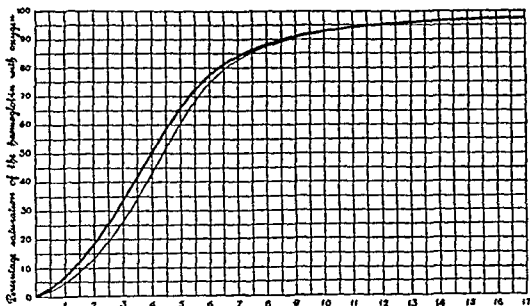


Fig. 2.—The thick line shows the dissociation curve of oxyhemoglobin in the presence of 40 mm. pressure of  $CO_2$ . The thin line represents the dissociation curve of oxyhemoglobin within the body. Abscissæ = pressure of oxygen in percentage of one atmosphere. (Haldane.)

is taken up by the tissues, oxyhemoglobin will give out oxygen following the same curve in the opposite direction. In this way considerable amounts of oxygen are liberated with only a slight drop in oxyhemoglobin saturation so that although one-third of the oxygen is used in the tissues, the venous blood is still 75 per cent. to 80 per cent. saturated with oxygen.

**Bohr Effect.**—The dissociation of oxyhemoglobin is influenced to a very considerable degree by the amount of  $CO_2$  present in the blood (Fig. 3). As the  $CO_2$  rises, the curve of oxyhemoglobin is shifted to the right, and, as  $CO_2$  decreases, the curve is shifted to the left. In other words, with higher amounts of  $CO_2$  in the blood, oxygen is liberated faster, whereas with low  $CO_2$  the oxyhemoglobin not only holds to its oxygen but also is saturated to a higher degree with oxygen of lower tension. This important phenomenon was observed by Bohr<sup>50</sup> and is called the "Bohr Effect." This Bohr effect explains a puzzling phenomenon often present in acute pulmonary diseases, or during the first post-

operative days especially after thoracoplasties; that is, deep anoxemia without or with slight and, rather "gray" cyanosis. This is due to the fact that in these cases shallow rapid breathing washes the very diffusible  $\text{CO}_2$  out of the alveolar air and the blood, without correcting the existing anoxemia. The result of this elimination of  $\text{CO}_2$  or acapnia (Henderson<sup>89 92</sup>) is a high saturation of hemoglobin notwithstanding the low tension of oxygen, so that the amount of "reduced hemoglobin" is not sufficient to produce a true cyanosis; furthermore a higher degree of anoxemia is produced due to the fact that oxyhemoglobin, in the absence of  $\text{CO}_2$ , does not give out its oxygen. A vicious circle is thus created, which, if not corrected, may lead to anoxemic death, as will be seen later.

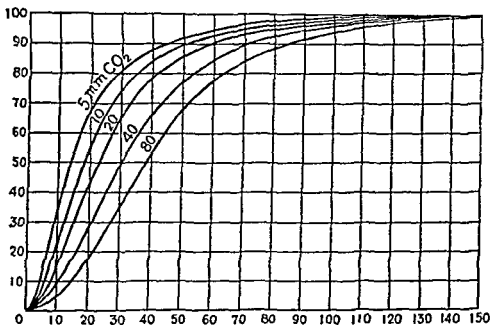


Fig. 3.—Curves representing the percentage saturation of hemoglobin with oxygen at different partial pressures of oxygen and  $\text{CO}_2$ . Dog's blood at 38 C. Ordinates = percentage saturation with oxygen; abscissæ = partial pressures of oxygen in millimeters of mercury. (Bohr, Hasselbach and Krogh.)

(c) **Dissociation of  $\text{CO}_2$** —Of still greater importance is the effect of the variations of  $\text{O}_2$  upon the curve of dissociation of  $\text{CO}_2$ . Because of the great solubility of the latter gas, its curve represents almost a straight line (Fig. 4) (Haldane). But whereas in the absence of oxygen the dissociation of  $\text{CO}_2$  will follow the upper line of Fig. 4, in the presence of oxygen under normal pressure it will follow the middle curve. This means that the elimination of  $\text{CO}_2$  will increase as oxygen increases. Therefore, elimination of  $\text{CO}_2$  from the blood is greatly facilitated during the passage of the blood through the pulmonary capillaries as its oxygen increases, and conversely, the absorption of  $\text{CO}_2$  by the blood becomes much easier in the tissues as oxygen is given off. So that while the venous blood is being aerated in the lungs (which is taking place between A and B in curve of Fig. 4), the absorption curve of  $\text{CO}_2$  will follow the thick line downward. It follows that 55 per cent. more of  $\text{CO}_2$  will be liberated than

if the lungs were not oxygenated. Werigo,<sup>131</sup> Bohr and Halberstadt<sup>58</sup> have shown that when one lung was aerated with hydrogen and the other with air, the lung ventilated with air gave off nearly 50 per cent. more  $\text{CO}_2$  than the lung ventilated with hydrogen. In this way the gas exchanges occur with but small variations in the partial pressures of the gases in the blood. Knowledge of these facts will aid in a more comprehensive interpretation of the regulation of respiration and of the importance of  $\text{CO}_2$  in this regulation.

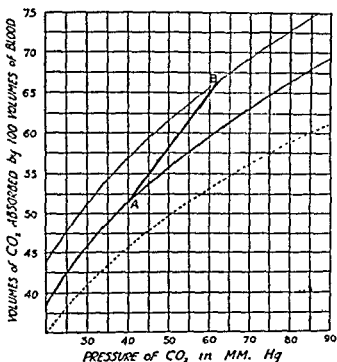


Fig. 4—Upper curve, absorption of  $\text{CO}_2$  by blood in presence of hydrogen and  $\text{CO}_2$ . Middle curve, absorption of  $\text{CO}_2$  by blood in presence of hydrogen and  $\text{CO}_2$ . Lower curve, absorption of  $\text{CO}_2$  in blood of ox and dog in presence of air and  $\text{CO}_2$ . (Bohr's data.) Thick line A-B represents the absorption of  $\text{CO}_2$  by the blood within the body. (Haldane.)

(d) *Regulation of Respiration.*—Breathing is regulated by the respiratory center, which coördinates the motor impulses to the respiratory muscles and constantly adapts them to the metabolic requirements of the organism. Conversely, the respiratory center is influenced by the chemical composition of the blood, by the peripheral centripetal nervous influxes and probably by chemical substances formed in the organism following oxygen want.

*Humoral Regulation.*—The “chemical” or the “humoral” regulator of respiration, by far the more important, is represented by the reaction of the blood or its hydrogen ion concentration ( $\text{pH}$  of the blood). As hydrogen ion concentration is especially dependent upon the amount of  $\text{CO}_2$  in the blood, it is generally considered that  $\text{CO}_2$  is the respiratory stimulus, although this point is still open to discussion.

Miescher<sup>111, 112</sup> in Germany, Haldane and Lorraine Smith<sup>56</sup> in England, Yandell Henderson and his collaborators in America,<sup>90, 95</sup> and since then a

great number of investigators, have shown the importance of both  $\text{CO}_2$  and  $\text{O}_2$  in the regulation of respiration. These authors have shown, that when rebreathing in a bag, in which oxygen is maintained at a steady level, hyperpnea will begin when the accumulating  $\text{CO}_2$  rises to 3 per cent. Hyperpnea gradually increases and becomes extreme as the  $\text{CO}_2$  approaches 10 per cent. Above this percentage stupefaction and narcosis occur. When, on the contrary,  $\text{CO}_2$  is absorbed in the rebreathing bag by soda-lime and the oxygen is not replenished as it is used up, no hyperpnea but tachypnea and periodic breathing followed by rapid shallow breathing will appear when the oxygen falls below 9 per cent. to 12 per cent.; these symptoms will increase greatly at lower oxygen percentages. With extremely low percentages of  $\text{O}_2$  in the inspired air, such as 2 per cent., consciousness is lost quite suddenly after 50 seconds of rebreathing and before any increase in the breathing rate has had time to develop (Haldane).

Thus, in the absence of any marked decrease of oxygen, deep breathing is due to increase of  $\text{CO}_2$ . This hyperpnea causes elimination of the excess of  $\text{CO}_2$  from the blood so that its amount is maintained strikingly steady, around 5.6 per cent. The respiratory center is so sensitive to any increase of  $\text{CO}_2$  that 0.23 per cent. rise in the alveolar  $\text{CO}_2$  gives a 100 per cent. increase in the alveolar ventilation. Conversely, after forced breathing for about one minute,  $\text{CO}_2$  is washed out of the alveolar air, and apnea occurs, which lasts about one minute and a half in man. A reduction in  $\text{CO}_2$  of as little as 0.2 per cent. is sufficient to cause apnea (Campbell, Douglas, Haldane and Hobson) which will last until the accumulation of  $\text{CO}_2$  brings this gas back to its normal amount. Thus the "astounding sensitiveness of the respiratory center to  $\text{CO}_2$  is established both in an upward and a downward direction; a mean increase or diminution of 0.1 per cent. in  $\text{CO}_2$  in the alveolar air will produce an increase or diminution of 50 per cent. in the alveolar ventilation of about 400 c.c. per minute in the lung ventilation" (Haldane). That this is due to the reduction of  $\text{CO}_2$  is proven by the fact that no amount of forced breathing will produce apnea when 5 per cent. of  $\text{CO}_2$  is constantly present in the air breathed.

*Variations of  $\text{O}_2$ ; Oxygen Want.*—What are the results of the variations in the amount of oxygen? Increase of  $\text{O}_2$  above normal in the alveolar air is of little if any importance upon the regulation of respiration in a normal animal. This is easily explained by the dissociation curve of oxyhemoglobin. It is a fallacy to believe, says Greene,<sup>83</sup> that by increasing the amount of oxygen in the air, even as much as 60 per cent., we will proportionately increase the content of  $\text{O}_2$  in the blood of a normal individual. As this author has shown, with 60 per cent. of  $\text{O}_2$  in the air breathed, oxygen will increase in the blood by only 1.25 per cent., which is of no value to a normal man "in whom the amount of oxygen in the venous blood is already from 13 to 15 c.c., that is, ten times greater." The above statement does not apply, of course, in pathological conditions of the lung.

Under high partial pressures (80 to 100 per cent. in the respiratory air) oxygen may cause inflammation of the respiratory membrane and edema of the lung. Haldane<sup>85</sup> reports a case in which fatal pneumonia was observed after continuous use of  $\text{O}_2$  at 73 per cent. for four days. When warm-blooded

or even cold-blooded animals are exposed to pure oxygen under a pressure of 3 or 4 atmospheres, they present tonic convulsions and die. This toxic action of  $O_2$  under high partial pressure was discovered by Paul Bert.<sup>55</sup> It is most remarkable that animals under these conditions present hypothermia and that, contrary to what would be expected, oxygen consumption and  $CO_2$  production are greatly diminished. When the partial pressure of  $O_2$  does not exceed 60 per cent., its use, even continuous for several days, is perfectly safe.

*Want of oxygen* leads, on the contrary, to the most severe complications. "Few things are more important in practical medicine," says Haldane,<sup>85</sup> "than effects of oxygen want." The effects of decrease of oxygen upon the respiration are much more marked when the reduction is produced rapidly than when the reduction is produced slowly.

Oxygen want in the systemic circulation may be produced in various ways; the two principal causes are decrease of oxygen "available" in the circulating blood, whatever may be its cause, and an abnormal slowing of the circulation which allows an exaggerated absorption of oxygen by the tissues.

The characteristic symptom of oxygen want is an increase in respiratory rate without increase in depth, that is tachypnea without hyperpnea. Although the beginning of tachypnea varies in different individuals it generally occurs when oxygen has dropped by a third. As anoxemia increases tachypnea will produce elimination of  $CO_2$ , and leads to periodic breathing. Further decrease of oxygen will produce fatigue of the respiratory center because of the anoxemia of its nervous cells which metabolize more rapidly than the other tissues of our organism and consequently are more sensitive to anoxemia (Parker<sup>117</sup>). This fatigue produces further increase in rate with a decrease in depth. Rapid shallow breathing is thus instituted which further increases anoxemia by a triple mechanism; it hinders adequate renewal of the alveolar air, causes insufficient expansion of the lungs leading to formation of unaerated channels (Keith<sup>102</sup>), and increases the elimination of  $CO_2$ . Because of the "Bohr effect" the remaining oxygen is firmly bound to the hemoglobin and becomes useless to the tissues. Anoxemia of the respiratory center is thus further increased, forming a vicious circle leading to anoxic crisis and death. Under these conditions the end can come without warning, without gasping for breath, without cyanosis, thus misleading the physician; moreover, misleading nervous and mental manifestations of euphoria and well-being develop and increase still further the seriousness of the condition. Unless these symptoms are well known and correctly interpreted, the patient is doomed and the few minutes left for successful action are lost by hesitation. Anoxic deaths are frequent in pulmonary tuberculosis following spontaneous pneumothorax or hemoptysis; in the latter, death is generally due not so much to the loss of blood as to the drowning and functional incapacitation of the lung.

Administration of  $CO_2$  in these cases of extreme emergency is indicated;  $CO_2$  releases the available oxygen in the blood by suppressing the Bohr effect and increases the depth of respiration. Any amount of pure oxygen given without  $CO_2$  may be useless because of the rapid shallow respiration and the Bohr effect. Therefore, I wish to state again, with Yandell Henderson,<sup>91</sup>

Haldane and Meakins<sup>87</sup> that to consider  $\text{CO}_2$  as a waste product which should be expelled, and to discuss lightly the uselessness of  $\text{CO}_2$  in anoxemia, can only denote ignorance of the interaction of  $\text{O}_2$  and  $\text{CO}_2$  and a confusion of "oxygen saturation of hemoglobin" with "free and available oxygen" in the blood. There is no doubt that insufficient knowledge on this point has done a great deal of harm in gas therapy, especially in lobar pneumonia.

*Oxygen Want.*—One of the following mechanisms or several of them together will produce oxygen want (Meakins and Davies<sup>110</sup>).

(A) Insufficient partial pressures of  $\text{O}_2$  in the inspired air (high altitudes, methane in mines with decreased percentages of  $\text{O}_2$ ).

(B) Obstruction of air passages or resistance to respiration.

(C) Obstruction to the passage of oxygen from the alveoli to the pulmonary blood (edema, inflammation, exudation, emphysema).

(D) Alteration of  $\text{O}_2$  carrying capacity of blood (anemia;  $\text{CO}$ , nitrite or chlorate poisoning).

(E) Circulatory failure.

(F) Pollution of oxygenated blood by mixing with the venous blood (uneven ventilation of the lungs as in tuberculosis, lobar pneumonia, bronchopneumonias, incomplete pneumothorax, pleurisy, and certain congenital heart diseases).

(G) When tissues are unable to utilize the oxygen brought to them by well oxygenated blood. (Cyanide poisoning.)

Only a few of the above mentioned causes will be touched upon, as having a special bearing upon pulmonary tuberculosis.

*Resistance to Respiration.*—Inadequate oxygenation of the alveolar air can be brought about not only by an insufficient amount of  $\text{O}_2$  in the air breathed, but also by resistance encountered in the passage of air in the larynx, trachea or bronchi. Increased resistance may play the leading part in the production of anoxemia in laryngeal, tracheal or bronchial stenosis; this may be due to organic lesions or more often to the presence of blood or exudate in the bronchial tree as following hemoptysis or thoracoplastic operations. Haldane, Meakins and Priestley<sup>87</sup> have shown that increased resistance to respiration, in clinical or experimental cases, caused a rise in  $\text{CO}_2$  in the alveoli and produced deeper and slower respirations. When resistance is further increased it leads to oxygen want in proportion to the resistance. Beyond a certain degree of resistance, the partial pressure of oxygen in the mixed alveolar air is inadequate to make up for the loss of oxygen in the tissues, and the respiratory center is affected, causing periodic and then shallow breathing; the latter produces excessive  $\text{CO}_2$  elimination, and leads to the syndrome of acapnia-anoxemia described above.

*Uneven Pulmonary Ventilation.*—Creates unaërated channels in the lung and promotes anoxemia. This is a phenomenon of importance in pulmonary tuberculosis. Bronchostenosis by bronchial lesions or bronchial compression by lymph nodes, or exudative or fibrotic thickening of the alveolar membrane (rendering it unsuitable for gas exchanges) may be the initial causes of oxygen want, producing respiratory changes in rate and depth, especially on exertion, often



out of proportion to the clinical findings (war gas poisoning). These phenomena easily explain the puzzling disappearance of dyspnea and a better oxygenation of the arterial blood after complete collapse of the diseased tuberculous lung by pneumothorax, as we shall see later. The importance of distribution of air in the lungs in the production of oxygen want was studied by Meakins and Davies<sup>110</sup>; in holding the breath for 40 seconds the hemoglobin in the blood of the radial artery was only 83.4 per cent. saturated with oxygen while the alveolar air contained a large amount of oxygen (13.4 per cent.). It is obvious that if this alveolar air were evenly distributed in the lung the hemoglobin should have been 97 per cent. saturated with oxygen.

Prolonged anoxemia, even if moderate, is a very dangerous condition. I wish to emphasize the point that prolonged anoxemia not only constitutes a serious menace to life, but also that its effect may persist long after the causes of anoxemia have been removed. This is clearly shown in CO poisoning, where the after-effects persist for many hours or even days and weeks after elimination of CO. It is known that CO produces simple anoxemia by combining with hemoglobin and displacing oxygen, as its affinity for hemoglobin is three hundred times greater than that of O<sub>2</sub>. It is an error to believe that CO is toxic; it is a neutral gas no more toxic than hydrogen or nitrogen; it passes through the lungs unchanged and is rapidly eliminated. It is peculiarly instructive to notice here the similarity between postasphyxial and postoperative pulmonary complications, especially following operations upon the chest for tuberculosis or other chronic suppurations of the lung. In the former anoxemia is due to the combination of hemoglobin with CO; in the latter anoxemia is due to prolonged resistance to respiration due to posture during operation, to presence of mucous exudate in the trachea and bronchi, and more especially to internal drainage of the bronchial exudate expressed from the collapsing diseased areas into the healthy bronchi (Faulkner<sup>78, 79 et al</sup>).<sup>\*</sup> Haldane, insisting upon the seriousness of increased resistance and of prolonged, even if only moderate anoxemia, says, in his textbook: "If there were only one clinical lesson derived from the perusal of this book, I hope that it would be that anoxemia is a very serious condition, the continuance of which ought to be prevented if at all possible."

*Acapnia.*—On the other hand carbon dioxide deficiency in addition to the serious respiratory disturbances already mentioned, gives rise to very important circulatory disorders. In fact, excessive elimination of CO<sub>2</sub> (acapnia) produces paralysis of the vasomotor centers and loss of muscular and vascular tonus, leading to stagnation of blood in the peripheral systemic arterial system; thus the amount of blood returning to the right heart is reduced; consequently the blood-pressure falls and the heart contracting on an amount of blood insufficient to fill it completely becomes fatigued and fails. The importance of acapnia in postoperative shock shown in a series of papers by Henderson and

<sup>\*</sup> In order to prevent anoxemia Coryllos<sup>66, 67</sup> uses for his thoracoplasties intratracheal anesthesia combined with suction of the mucous exudate accumulating in the bronchi during the operation.

Haggard,<sup>94</sup> has been recently studied by Coryllos<sup>95</sup> in the hemorespiratory postoperative complications following thoracoplasties.

*Nervous Regulation of Respiration—Hering-Breuer Reflex.*—In the regulation of respiration, besides the chemical factors studied above, an important part is played by peripheral stimuli carried to the nerve center through almost every one of the centripetal nervous fibers and more especially through the vagi. Hering and Breuer<sup>99</sup> have shown (1868) that inspiratory dilation of the alveoli inhibits inspiration and starts expiration, and on the contrary, expiratory collapse of the alveoli inhibits expiration and starts inspiration. With the vagi intact this reflex is greatly influenced by variations of  $\text{CO}_2$  and  $\text{O}_2$ . When both vagi are anesthetized, frozen, or sectioned, the reflex disappears and the respiratory rhythm is no longer associated with the discharges of the center; neither inflation or deflation of the lungs nor variations of oxygen or  $\text{CO}_2$  any longer have any great influence upon the respiratory rhythm. Periodic, rapid shallow breathing and Cheyne-Stokes respiration disappear by freezing or section of the vagi.

(e) *Gas Exchanges in the Pleural Cavity.*—It is obvious that gas exchanges in the pleura follow the same fundamental laws as gas exchanges in the lung. This statement, however, brings in the question of negative intrapleural pressure, of absorption of gases artificially introduced into the pleura, and, on the other hand, of spontaneous production of pneumothorax after death. In fact, peculiar as it may appear, no clean-cut explanation has thus far been given for the following phenomena, which are apparently in contradiction to the law of partial pressures: (1) that the air contained in the lung does not diffuse into the pleural cavity where partial pressures of the same gases certainly are lower since the pressure in the pleura is subatmospheric; (2) that the gases of artificial pneumothorax are gradually absorbed, and (3) that, on the contrary, after death air diffuses through the pleural layers into the pleural cavity, producing a postmortem pneumothorax.

A plausible explanation of these phenomena, based on experimental data, was given by Rist and Strohl<sup>121-123</sup> and more recently by Coryllos and Birnbaum.<sup>68-71</sup> These authors showed that during life gases diffuse through the visceral pleura but are constantly absorbed by the circulating blood according to the same mechanism by which alveolar gases are absorbed following bronchial obstruction; the same physiochemical laws account for the absorption of gases injected into the pleura, the peritoneum or the subcutaneous tissues or contained in tuberculous cavities when their draining bronchi become obstructed. This mechanism is in perfect agreement with the general laws of gas exchanges as will be shown in the following chapters, in which the pathologic-physiologic questions outlined above will be answered in detail.

### III. PATHOLOGIC PHYSIOLOGY.

(A) *Gas Absorption in the Obstructed Lung and in the Pleural Cavity—Obstructive Atelectasis and Obstructive Emphysema.*—Gas absorption, both in an obstructed portion of the lung and in the pleural cavity, will be studied together because, although it may appear strange at first sight, they

are physiologically identical (Coryllos and Birnbaum<sup>66 69</sup>). Exact knowledge of these phenomena is of great importance to the phthisiologist. As far back as 1879 it was known (Lichtheim<sup>106</sup>) (it was suspected even previously to that date) that obstruction of a large bronchus, if prolonged for a sufficient length of time, leads to the absorption of the air contained in the portion of the lung corresponding to that bronchus, and that this portion of the lung takes on the aspect, consistency, texture and specific gravity of the fetal lung. This condition has been designated as atelectasis or even better as apneumotosis (airlessness). It seemed reasonable to surmise that this absorption was accomplished by the blood circulating in the alveoli; in fact, it had been shown (Lichtheim<sup>106</sup>) that if the branch of the pulmonary artery corresponding to the obstructed bronchus was ligated atelectasis did not occur. The detailed and intimate mechanism of this absorption has, however, been worked out experimentally only recently by Coryllos and Birnbaum,<sup>66 69</sup> who have investigated on the dog the changes occurring in the gaseous content of the obstructed lobe beyond the bronchial obstruction. They have formulated a theory, generally conceded, which is summarized in the legend to Fig. 5.

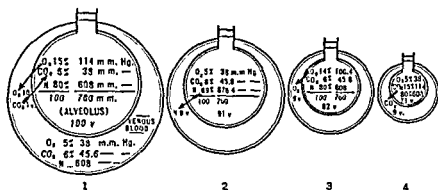


Fig. 5.—A schematic representation of alveolar gas exchanges, gradual gas absorption and shrinkage of the alveoli after complete bronchial obstruction. The absolute volume of the alveolus is only approximately indicated, but the figures are relative and demonstrate perfectly well the principles involved. In 1, 10 volumes of oxygen diffuse into the venous blood and 1 volume of carbon dioxide diffuses out of the venous into the alveolus. In 2, the alveolus has now lost 9 volumes of gas as stated under 1 and oxygen and carbon dioxide have come into equilibrium in the venous capillary blood and in the alveolus. However, the percentage and partial pressure of nitrogen have now been increased so that 9 volumes of nitrogen diffuse out of the alveolus into the venous blood. In 3, 9 volumes of nitrogen having previously diffused out of the alveolus into the venous blood, the percentage and partial pressure of oxygen or carbon dioxide have been relatively increased. For purposes of explanation let us say the oxygen has thus been relatively increased in percentage and partial pressure. Nine volumes of oxygen are now ready to diffuse out of the alveoli into the venous blood. In 4, 9 volumes of oxygen having diffused from the alveolus into the blood, we can consider that the carbon dioxide in the alveolus is relatively increased by these 9 volumes. Thus the partial pressure of this gas is relatively increased and carbon dioxide is ready to diffuse out of the alveolus. Thus the cycle continues until all the gases of the lungs are absorbed, although, actually, the gas exchanges are going on simultaneously and not in the isolated way which we have ideally considered. (Coryllos and Birnbaum.)

This conception renders perfectly clear the mechanism of production of atelectasis whenever and wherever a larger bronchus is obstructed. It also explains the frequent production of atelectasis in pulmonary tuberculosis; in fact, in this disease the lesions of the bronchi, be they exudative, caseous or productive, are constant and early, easily leading to their partial or complete obstruction. It was shown that atelectasis cannot be produced unless there is a complete bronchial obstruction. When a simple stenosis is present three things may occur. Either (1) the bronchus may remain permeable to the respiratory air during both inspiration and expiration; or (2) the bronchus may become completely occluded by allergic edema, granulations or scar tissue, by caseous material, by thick bronchial secretions or by blood following hemoptysis; or (3) the bronchus may remain patent during inspiration but collapse and close during expiration, forming a check-valve mechanism (Jackson<sup>99a</sup>). In the first case nothing will happen; in the second the corresponding part of the lung will become atelectatic; and, in the third instance, obstructive emphysema (Manges) will develop.

This conception, based upon simple and fundamental laws, is closely applicable to gas exchanges and gas absorption in the pleural cavity. There can be no doubt that a continuous diffusion of gases takes place from the lung into the pleura during life; however, these gases are continuously absorbed by the circulating blood and by the same mechanism by which air is absorbed in the peritoneum or the subcutaneous tissues. On the contrary, with the arrest of circulation, after death the physical phenomena of diffusion of gases from higher towards the lower pressures are not counterbalanced by the absorption of these gases, so that the air diffuses from the lung into the pleura, forming the well-known postmortem pneumothorax. This establishes beyond any reasonable doubt the rôle of circulating venous blood in the production and maintenance of the pleural subatmospheric pressure and in the absorption of air, artificially or accidentally, introduced into the pleural cavity. This conception throws a new light upon the physiology of the pleura and, more important, establishes the identity of the pathologic physiology of phenomena up to now considered completely unrelated, such as: pulmonary atelectasis and obstructive emphysema, closed and open pneumothorax, and closed and open tuberculous cavities of the lung. To me, this likeness is striking and illuminating because a great number of problems heretofore puzzling and inexplicable can be solved, as we shall see, with the greatest ease.

Gases injected into the pleural cavity are gradually absorbed as gases contained in a lobe are absorbed when the bronchus to that lobe is obstructed. The speed of their absorption depends upon three factors: the nature of the gases, the permeability of the pleura, and the activity of the circulation. The speed of the absorption of a great number of gases has been studied by Coryllos and Birnbaum<sup>68</sup> both in the lung previously rendered atelectatic and in the pleural cavity, in the human<sup>71</sup> as well as in a number of laboratory animals; it was constantly found that this absorption follows the fundamental laws of diffusion, solubility, and partial pressures which regulate gas exchanges. In the order of decreasing speeds of absorption they were classified as follows: carbon dioxide.

nitrous oxide, ethylene, ethyl chloride, ether vapor (not over 30 per cent. concentration), oxygen, nitrogen, hydrogen and helium.

The likeness between the pulmonary and the pleural absorption goes further. In cases of open pneumothorax communicating with the outside world either through a pleuro-pulmonary fistula or an opening in the chest wall, the air is constantly renewed and thus cannot be exhausted although continuously pumped out by the blood, exactly as in the normal lung with patent bronchi. Any lack of balance between ingress, egress and absorption of air, will be followed either by the increase of negative pressure or by tension pneumothorax in the pleura, as in an exactly parallel manner it is followed by atelectasis or obstructive emphysema under similar conditions in the lung.

(B) *Tuberculous Cavities.*—Massive bronchogenous infection with tubercle bacilli, followed by caseation and elimination of the necrotic material through the bronchi, leads to the formation in the lung of excavations or rather tuberculous abscesses, which are separated from the lung parenchyma by a membrane of variable thickness. When their caseous content has been emptied through the bronchi they represent "holes" in the lung which communicate with the bronchial tree through one or more "draining bronchi."

*Problems.*—Numerous problems which are related to cavities and are of the greatest interest to the phthisiologist are still open to discussion. In the following, only four problems will be considered.

1. Why are the cavities spherical in the living, whereas on the autopsy table they appear irregular in shape?

2. What is the mechanism of their closure, be it spontaneous, or following collapse treatment?

3. What are the causes, besides very thick walls, which may prevent their closure by artificial collapse either by pneumothorax or even by thoracoplasty; and how can the fact be explained that in the presence of pneumothorax a few tiny adhesions can prevent closure of the cavities or that they may even increase in size although they are completely surrounded by the air of the pneumothorax?

4. By what mechanism do cavities increase in size, sometimes very rapidly, without any radiographic signs suggesting extension of the lesions and sloughing out of a tuberculous parenchyma?

The mechanism of formation of a tuberculous cavity can be likened to the formation of an abscess anywhere in the organisms, whatever its bacteriology may be; however, "tuberculous abscesses" in the lung present a number of special features due only to the special characteristics of tuberculous infection and of the organ in which they develop. Let us recall here that the lung is the only organ of our body which is inflated with air constituting  $\frac{2}{3}$  of its volume, so that any interference with the patency of the bronchi will immediately lead to considerable change in its volume; that is decrease and collapse in atelectasis or increase with distention in emphysema. For that reason, changes in the size of the lung following inflammatory lesions are regulated, contrary to what occurs in organs which are solid and fixed in size, by the variations in the amount of air present in that organ. It is because this important factor in pathologic physiology of the lung has been neglected that we have been at a loss to explain

phenomena and symptoms which seem to disagree with the general laws of general pathology, such as decrease in size of this organ in acute inflammatory lesions and even in tumors, where the inflammatory edema, or the neoplastic infiltrations are counterbalanced and overshadowed by the atelectatic shrinkage of the lung due to bronchial obstruction. This neglect also explains why so many



Fig. 6.—Pathological specimen, Sea View Hospital. Drawing bronchi of cavities. Probes are introduced into the bronchi.

fancy and unwarranted theories have prevailed so far. I shall come back to this point later.

The *special characters* of the tuberculous cavity are, I believe, closely connected with the draining bronchi, through which the cavity communicates with the bronchial tree and through it with the outside world; these bronchi are easily located in the specimen (Fig. 6) and often are apparent in the radiograms; in the latter often the cavities assume the form of a tennis racquet, the draining bronchus

representing the handle. These cavities have been named Stiel-Kavernen by the German authors; I shall designate them by the name of Stem-Cavities. It is peculiar that no special attention has been given to these connecting or draining bronchi whereas such thorough and detailed study of and discussion on the characters and significance of the walls of the cavities have been carried on. Clinical and experimental investigation, so far only partially reported,<sup>72\*</sup> have convinced me that these bronchial outlets constitute the most important factors in the evolution of cavities. In fact, these draining bronchi show in the pathological specimen, more or less advanced but always present tuberculous lesions, which vary from allergic edema to caseous and necrotic alterations or productive fibrous changes. All these lesions tend to produce stenosis and often cause complete obstruction. On the contrary, in some cases these bronchi show an advanced degree of sclerosis so that they remain patent and offer considerable resistance to collapse as do arteriosclerotic arteries. The elucidation of these points will go a long way toward facilitating the answers to the problems raised at the beginning of this chapter.

1. The spherical shape of the cavity is due simply to the differences in pressures inside and outside of the cavity. Inside the cavity the pressure is equal to that of one atmosphere so long as the cavity communicates freely with the outside world. Around the cavity, the pressure is equal to the intrapleural pressure, which is normally  $-7$  mm. Hg. and very often much more negative (from  $-7$  to  $-30$  mm. Hg.) owing to the atelectatic and fibrotic shrinkage of the surrounding parenchyma. Thus the pressure being lower outside than inside, or, one may say, higher inside than outside, the cavity is compelled for obvious mechanical reasons to assume a spherical shape. The question is so simple that one wonders why so many and so complicated explanations have been proposed. Tuberculous cavities are spherical for the same reasons that abscesses in any part of our soft tissues are spherical.

2. The evolution of the cavity will depend upon the pathologic and mechanical changes which may occur in its draining bronchus or bronchi.

In fact, three things may happen to this bronchus—*First*, it may remain patent. In that instance the cavity will preserve its shape and most often its size. *Second*, it may become obstructed. In this case the air contained in the cavity will be gradually absorbed by the same mechanism as in atelectasis following bronchial obstruction, or as in the pleural cavity in closed pneumothorax and the cavity will shrink and disappear. *Third*, a check-valve mechanism may develop, allowing free ingress of air but not free egress. In this case the size of the cavity will increase exactly as the lung is distended in obstruction emphysema and the pleural cavity in tense pneumothorax.

To support this conception there is abundant pathological, clinical, radiographic and experimental evidence.

We have seen in the mechanics of respiration that the bronchi, and especially the small ones, expand during inspiration and contract during expiration. The degree of their inspiratory dilation and expiratory collapse depend upon the

\* Extensive bibliography will be found in this paper, page A-194 et seq

depth of breathing and the tonus of the bronchial musculature. In quiet breathing these changes are naturally much less marked than in deep breathing and in decubitus less than in the erect position. It is obvious that, because of the more or less advanced tuberculous lesions of the bronchi, not only is their elasticity impaired but also a variable degree of stenosis is almost always present. Loss of elasticity of the bronchial walls will handicap inspiratory enlargement and elongation of the bronchi, which leads, as Macklin<sup>100</sup> has shown, to limitation of inspiratory expansion of that portion of the lung (see Mechanics of Respiration). Furthermore, inflammatory anchoring of the hilum will further immobilize the supero-retro-radicular region of the lung and for that reason 90 per cent. of all the cavities are located in the apices. Complete rest in decubitus causes a considerable reduction of inspiratory pulmonary expansion, which, for reasons given above, is more marked in the involved bronchi and bronchioli. This is, I believe, the mechanism by which bed rest produces a *selective respiratory rest* of the affected parts of the lung. This conception easily explains the production of defective ventilation in the diseased lung and the creation of unaerated channels. The latter are shown by the increased  $\text{CO}_2$  and decreased  $\text{O}_2$  in the arterial blood, and, conversely by the rapid reestablishment of their normal percentages after an adequate therapeutic collapse or spontaneous fibrotic shrinkage of the diseased lung has occurred which stops circulation in the diseased areas. Moreover, decreased ventilation is accompanied by decreased drainage, so that mucous plugging of the diseased bronchi becomes easier. Additional immobilization of the chest, as by placing weights on it or by pneumothorax or thoracoplasty, further increases the chances of collapse and closure of the bronchial outlets, with consequent absorption of the air content and collapse of the cavity. The speed of air absorption and collapse depends, of course, upon the permeability of the walls of the cavity to gases, upon the activity of circulation in the walls and the pulmonary area surrounding the cavity and upon their mechanical resistance to collapse. It is obvious that in thin-walled cavities in which these three requirements are fulfilled, absorption and collapse will be more rapid than in old cavities with thick walls and with circulation cut off in the surrounding atelectatic and fibrotic parenchyma. Thus it is not merely the mechanical resistance of their walls to collapse that renders old cavities difficult to collapse, but also their decreased permeability to gases and absence of circulation. There are, of course, cavities with extremely resistant and even calcified walls or which are strongly adherent to the chest wall, with sometimes the whole apex "shelled out," which obviously cannot collapse even when their draining bronchus is closed. These cavities resemble pneumothorax with very thickened or calcified pleura in which air may persist indefinitely without any refills. It is exactly for the opposite reasons that annular shadows, be they very young cavities or bulbous obstructive alveolar emphysema, respond so promptly to rest or collapse treatment and even disappear spontaneously. On the other hand the increase in the size of the cavities, often without any apparent change in the surrounding parenchyma indicating extension of the lesion, is easily explained by the formation of a check-valve mecha-



nism in the stenosed and irregular lumina of their bronchial outlets, leading to "obstruction emphysema" and ballooning of the cavity.

The above elaborated theory, besides its physiological foundations, is further corroborated by clinical evidence. First, that often, shortly after successful pneumothorax or thoracoplasty, the sputum becomes negative. It is evident that this can be explained only by the closure of the draining bronchus of the cavity. Second, that when in pneumothorax even a few thin adhesions are present, the cavity remains open although it is submitted to the collapsing action of the air present all around it. It is a peculiar fact, never pointed out previously so far as I am aware, that the adhesions which most effectively interfere with collapse of the cavity have a constant direction, up and backwards towards the second and third intercostal spaces and the posterior axillary line. It is well known to surgeons who have had experience with closed pneumolysis method of Jacobaeus that these adhesions are precisely the ones which must be divided and after the section of which the cavity usually closes. Can it be mere coincidence that the direction of these adhesions represents the prolongation of the apical bronchus, so that they keep this bronchus straight and prevent its collapse or kinking when the apex drops to the level of the hilum as usually occurs following successful pneumothorax?

Manometric readings and gas analysis of the air of cavities, performed upon a number of patients at the Metropolitan Hospital of New York,<sup>71</sup> have further substantiated this conception. In rapidly expanding cavities the pressure was regularly found positive (+2 to +4); the oxygen was lower (around 12 per cent.), whereas the carbon dioxide was always higher (around 0.5 to 2.0 per cent.) than in the outside air. This shows that the air was more or less entrapped in the cavity and only partly renewed. On the contrary, in cavities with open bronchial outlet the pressure was found equal to atmospheric (-1+1) and the air contained in them had a composition similar to the outside air, richer in oxygen and poorer in carbon dioxide than the alveolar air (O<sub>2</sub> 17 to 19 per cent., CO<sub>2</sub> 0.5 to 1.0 per cent.).

(C) *Atelectasis and Fibrosis in Pulmonary Tuberculosis.*—The above conception offers, I believe, a well grounded and physiological explanation of the production of atelectasis in tuberculosis and of the ease with which fibrosis develops in the tuberculous lung.

Atelectasis is of frequent occurrence in pulmonary tuberculosis (Jacobaeus,<sup>100, 101</sup> Packard,<sup>114, 115, 116</sup> Farris,<sup>77</sup> Gatterdam,<sup>80</sup> Hennel,<sup>98, 97, 98</sup> Stoloff,<sup>127</sup> Glenn<sup>81</sup>), because of the frequency of bronchial obstruction in that disease, produced by one of the mechanisms studied above. It is fairly well proven today that a great number of cases formerly diagnosed as fibrotic lungs are really atelectatic; it is because fibrosis follows very closely atelectasis that in the pathological specimen it is not always possible to determine their respective parts in the shrinkage of the lung and even less to establish which had developed first. Therefore, atelectasis is more evident in children, because at that age fibrosis rarely develops.

In the living patient clinical differentiation between atelectasis and fibrosis is often possible; in a considerable number of reported cases lesions, lobar in

distribution and affecting one or more lobes, were shown in serial roentgenograms to appear within a few days and to disappear as rapidly. In more prolonged cases bronchoscopic examination showed the presence of granulating or scar tissue obstructing the bronchus (Myerson\*). Clinically these cases presented all the symptoms of atelectasis, namely dullness, decreased or absent breath sounds or transmitted bronchial or tracheal sounds, displacement of the trachea, heart and mediastinum and elevation of the diaphragm on the affected side. We must concede that fibrosis cannot develop in such a short time and cannot disappear once it has developed. The question of atelectasis in pulmonary tuberculosis, incompletely studied so far, is of far greater importance than is generally believed. I firmly believe that it is so closely related to the mechanism of cure of the disease that it is worth persistent emphasis.

*Relation.*—Atelectasis acquires particular importance in its relation to the subapical lesions of Assman,<sup>53</sup> which, according to Scheidemandel<sup>123</sup> and others, represent around 40 per cent. of the early localizations of the disease. In many acute manifestations marking the beginning of the disease and generally diagnosed as colds, grippe, or pneumonia, radiograms have shown the presence of these subapical lesions. Their radiographic characteristics are of interest; sometimes isolated patches, they more often assume a wedge-like shape with its base directed toward the periphery. There is a tendency to more or less marked displacement of the trachea to the affected, but never toward the healthy side. When they are more extensive even the diaphragm and the heart may be displaced towards the affected side. There are scanty stethoscopic signs apart from a slight dullness present in some cases; breath sounds are decreased and râles are absent. Their appearance is often sudden; likewise their disappearance may occur within a few days or weeks. Their nature and pathogenesis are subject to discussion. For Eliasberg and Neuland<sup>76</sup> and others they are epituberculous infiltrations caused by superinfection with ordinary microorganisms; for Ranke<sup>119</sup> they represent perifocal inflammations around a central tuberculous process, and a dense area of exudation into the parenchyma. Reichle<sup>120</sup> in a recent paper, studying what he calls "Resolving Exudates in Pulmonary Tuberculosis," concludes that there are three types of subapical lesions. (1) Atelectasis, (2) nontuberculous lobar or bronchopneumonia, and (3) retrogressive tuberculous pneumonia.

The above conceptions do not, however, explain the shrinkage of the lung as a result of an acute inflammatory process; nor do they make clear the mechanism of the frequently encountered clean-cut limitation of the process in the midst of apparently healthy pulmonary tissue. We are thus faced with apparent contradictions similar to those encountered in the pathogenesis of lobar pneumococcic pneumonia in which the lobar localization of the disease, the decrease in the size of the diseased lung, notwithstanding the acute inflammatory process, had remained unexplained until recently.

As in lobar pneumonia, I think<sup>70</sup> that the explanation of the pathogenesis of these infraclavicular tuberculous lesions is to be looked for in the pathologic

\* Not yet published. Personal communication.

physiology rather than in the pathology of the diseased lung, especially since postmortem data are rare in these stages of the disease. I believe that here again we are dealing with bronchial obstruction, lobar or lobular, produced by allergic edema of the bronchial mucosa.\* This hypothesis explains the sudden appearance and disappearance of these lesions, their distribution, and especially the shrinkage of the lung, the retraction of the structures of the mediastinum towards the affected side and the absence of stethoscopic signs. In fact in any other organ allergic manifestations are always accompanied by "edema," and enlargement and never by decrease of the size and shrinkage of the affected area. It is the same with all diseases of the lung, inflammatory or neoplastic whenever they are accompanied by bronchiolar or bronchial obstruction; that is, although the size and the weight of the parenchyma of the lung *increases* the size of the diseased lung *decreases*. This statement which would be a paradox if applied to any other organ is perfectly true with the lung; it is easily explained by the absorption of air and atelectasis which take place in the lung under these conditions, and the fact that  $\frac{2}{3}$  of the size of the lung is represented by air. Thus increase in size of the parenchyma *per se* and of the weight of the diseased lung are by no means contradictory to the decrease of the volume of the diseased portion of the lung.

The further evolution of these early tuberculous lesions can be satisfactorily explained by the same theory. In fact during the atelectatic period only the functional circulation of the affected area, that is, the circulation in the alveolar capillaries fed by the pulmonary artery, is impaired, whereas, the nutrient circulation insured by the bronchial vessels remain normal; therefore no necrosis of the pulmonary parenchyma will occur. So that when the allergic phenomena recede before any serious and permanent damage has been done to the nutrient vessels, complete reëration of the lung parenchyma may occur as the allergic bronchial edema subsides and the obstructed bronchi become patent. On the contrary, when the dosage is sufficient to produce an inflammatory reaction causing permanent damage to the vessels and the tissues, ischemic necrosis and toxemic caseation will follow. Between these extreme forms we find mixed forms in which one or the other of these conditions, allergic or necrotic, predominates.

*Significance.*—It is my opinion that atelectasis is a phenomenon which complicates pulmonary tuberculosis, as it does any other pulmonary disease, only when bronchial or bronchiolar occlusion is present, regardless of the nature, bacteriology or pathology of the disease which has produced it. However, in a number of pulmonary diseases atelectasis is of paramount importance in the development and evolution of the disease itself; two diseases seem especially influenced by atelectasis, namely tuberculosis and anaërobic infections. The latter, because anaërobic organisms cannot develop and grow unless previous bronchial obstruction and atelectasis have deprived the pulmonary tissues of the considerable amount of oxygen contained in it. Tuberculosis, for exactly the

\* This conception has been confirmed lately by the Bronchospirometric Studies of Stig Björkman (Acta Scandinavica, Supplem. 41. Stockholm, 1934).

opposite reasons, namely, that absorption of oxygen following atelectasis hampers and even stops further development of tubercle bacillus, as will be shown below.

*Fibrosis.*—It is known that tuberculosis is a great promoter of fibrosis. Leriche and Polcard believe that this is because tuberculosis is exclusively a disease of the connective tissue, and also because it produces early and marked vascular lesions. The morphologic elements of the disease, the tubercles, are *deprived of circulation, being avascular formations*. On the other hand, it is known that ischemia and anoxemia of the tissues favors fibrosis. In the ischemic myositis or paralysis of Volkmann the muscles may become fibrotic following application of a tight cast on the arm for a week or so; the same, prolonged immobilization promotes the development of fibrous tissues in joints and muscles. Whatever may be the cause of these lesions: *mechanical ischemia, venous stasis or reflex nervous vasoconstriction, it seems that the important factor in their production is always lack of an adequate amount of oxygen to carry on the normal metabolic processes*. Atelectasis in the tuberculous lung acts by the same mechanism; it causes the suppression of circulation in the tuberculous lung, and thus leads to tissue anoxemia and fibrosis. This hypothesis would explain the action of rest and more especially of collapse of the lung in the production of fibrosis and cure of tuberculosis. It would help also to understand the curious phenomenon of limitation of fibrosis to the diseased portions of the lung following pneumothorax, while the healthy lung can remain collapsed for a long time without presenting any marked fibrotic changes; in fact in the diseased areas both functional and nutrient circulation were suppressed, whereas in the healthy lung the nutrient circulation had remained intact. This connection of atelectasis with fibrosis is of importance because it throws a new light upon the intimate mechanism of cure of pulmonary tuberculosis.

**Mechanism of Cure of Pulmonary Tuberculosis.**—Recent studies of the biology and more particularly of the respiratory metabolism of the tubercle bacillus, especially of the virulent human species, have shown (Novy and Soule,<sup>113</sup> Loebel, Schorr and Richardson<sup>108</sup>) that this organism is a strict aërobe, and furthermore that it requires large amounts of oxygen for continuation of life and growth. Contrary to the facultative aërobes or anaërobes, tubercle bacilli not only do not grow in absence of oxygen, but need considerable amounts of it for continuation of life, three times more than equal weights of muscle of a dog at rest (Novy<sup>113</sup>). In the absence of oxygen the respiratory metabolism of human tubercle bacillus H37 rapidly falls to zero; within 4 to 8 days, growth stops and recultivation becomes problematic (Loebel, Schorr and Richardson<sup>108</sup>).

It therefore seems permissible to advance the hypothesis that in the course of pulmonary tuberculosis every factor which tends to decrease or suppress the supply of oxygen carried to the diseased areas by the respiratory air and the circulating blood will produce at the same time a serious impairment of growth and vitality of the tubercle bacillus. The causes responsible for the production of anoxemia of tuberculous lung are: on one hand the vascular lesions due to

the disease and on the other atelectasis; the latter suppresses both sources of oxygenation in the affected areas, i. e., respiration and circulation.

This conception places rest and collapse treatment of tuberculosis on a rational and physiological basis. Moreover it offers a scientific explanation of the cure of the disease following collapse of cavities. In fact, following closure of the draining bronchus of a cavity the air contained in it, and especially the  $O_2$ , gradually disappear. The absorption of  $O_2$  by the cellular tissues is more rapid than would be suspected and this because of the extraordinary affinity of the avascular tuberculous tissues for  $O_2$  (Novy,<sup>113</sup> Warburg<sup>128 129</sup>). Absorption of  $O_2$  produces a condition of anoxemia in which tubercle bacillus cannot grow.

It is certainly too early to evaluate the merits of this theory. At any rate it is the first time that a conception based on unimpeachable physiological and biological evidence has been advanced for the explanation of cure of tuberculosis by rest, pneumothorax or thoracoplasty, and that evidence has been offered showing that these three fundamental methods of treatment are based upon the same principles of pathologic physiology.

**Intrapleural Pressures.—Their Effects Upon the Tuberculous Lung. Pneumothorax-Gas Analysis of Pleural Gases and Its Practical Application. Thoracoplasty.—Intrapleural Pressures.**—As has been shown above, the subatmospheric pressure in the pleural cavity measures on the average  $-7$  mm. Hg. under normal conditions. This does not mean that there is a "vacuum" in the pleura but simply that the pressure in it is  $760 - 7 = 753$  mm. Hg., if the atmospheric pressure is 760 mm. Hg.

This "negative pressure" is equal to the strain exerted by the elastic recoil of the lung. Intrapleural pressure and elastic recoil of the lung are necessarily in constant equilibrium with each other. In other words when the intrapleural pressure increases (becomes less negative), the elastic recoil of the lung decreases and the lung collapses proportionately to the increase of intrapleural pressure. Conversely, when the degree of expansion of the lung decreases as in atelectasis or fibrosis, the intrapleural pressure tends to decrease, all other factors remaining the same. For these reasons, when we know one of these two factors, we can easily deduce the other.

In artificial pneumothorax, however, this simple mathematical relation is disturbed by the introduction of a number of varying factors which are: gas exchanges and gas absorption in the pleural cavity; changes in the permeability of the pleura to the gases; variations in the blood circulating beneath the visceral pleura; and, above all, changes in the ability of the underlying lung to expand. These varying factors, although closely interrelated, should be considered separately; accurate knowledge of them is indispensable for the comprehension of the apparently involved pathologic physiology of artificial pneumothorax.

(a) *Gas Exchanges and Absorption in the Pleura.*—As has already been shown, gases diffuse from the air of the pneumothorax into the venous blood, and *vice versa*, tending to establish an equilibrium between their partial pressures in the two media. Immediately following introduction of air in the pleura, carbon dioxide, which is the most diffusible of the gases present, rushes from the venous

blood into the pneumothorax as its partial pressure in the blood is about 6 per cent. of one atmosphere whereas in the atmospheric air of the pleura is almost *nil* (0.03 per cent. of an atmosphere); it is thus evident that the volume of the air in the pleura immediately following the production of pneumothorax will increase (Dautrebande and Spehl,<sup>74</sup> Rist and Strohl<sup>121</sup>). However, in the meantime  $O_2$ , the partial pressure of which is 20.49 per cent. in the pneumothorax and only 5 per cent. of one atmosphere in the venous blood, will begin to diffuse into the blood, so that within one or two hours after the introduction of air into the pleura, the total volume of pneumothorax will be found decreased. Thus it becomes clear that whatever gas we introduce into the pleural cavity,  $N_2$ ,  $H_2$ , helium or air, after a short while we shall find in the pleura  $O_2$  and  $CO_2$  under the same partial pressures as in the venous blood circulating under the pleura. Therefore the only difference between pneumothorax induced with  $N_2$ ,  $H_2$ , or helium, and pneumothorax with air, consists in the slower absorption of these gases because of the absence of oxygen and  $CO_2$  in the initial gas mixture.

A perfect and steady equilibrium between the venous gases and the pleural air is never realized because of the enormous differences in diffusion speeds between  $CO_2$ - $O_2$  and  $N_2$ . Therefore, according to the mechanism already studied,<sup>68</sup> which regulates gas absorption in the obstructed lung, gases present in the pleural cavity will be gradually absorbed completely. In fact, it is quite impossible to produce pneumothorax with  $CO_2$  because this gas is absorbed almost as quickly as it is introduced or with  $O_2$  which although it is absorbed 25 times slower than  $CO_2$ , it is still absorbed too rapidly to be used for pneumothorax.

(b) *Permeability of the Pleura to Gases.*—The speed of gas absorption varies with the anatomical condition of the pleura. Healthy, thin and well vascularized pleura is readily permeable to gases; on the contrary, chronically inflamed and thickened pleura (prolonged pneumothorax, pneumothorax with empyema, calcified pleura) is less permeable and may become impervious; this explains the rapid absorption of the air of pneumothorax following the first few refillings and its slowing down in subsequent ones.

(c) *Variations in the Circulation Beneath the Pleura.*—This is one of the most important factors in the regulation of absorption of pneumothorax. Because of the great richness of pulmonary circulation as compared to the circulation of the chest walls, it is obvious that gas exchanges through the visceral pleura are incomparably more important than through the parietal pleura. In the following we shall consider only the former. This circulation varies with and proportionately to the condition of the underlying lung; it is maximum in the healthy and expanded lung and minimum in the collapsed and especially in the atelectatic one. As we have seen above, collapse of the alveoli causes a parallel collapse of the alveolar capillaries so that ventilation and circulation decrease together. It is obvious that diminished blood flow beneath the pleura will cause slower absorption of the pleural gases. Consequently, as the collapse of the lung increases in proportion to the amount of air introduced in the pleura, the speed of absorption of gases will vary in inverse proportion to the latter. When pressures in the pleura approach or become equal to one atmosphere, the elastic recoil of the lung decreases and gradually becomes *nil*; as the lung collapses,

its functional circulation decreases until it is represented almost exclusively by the blood circulating in the bronchial arteries and veins. This, however, does not occur until the air entrapped in the collapsed lung has been completely absorbed and the lung has become atelectatic. Until then, circulation in the partially collapsed and unevenly ventilated lung is continued; the blood passing through unaerated channels arrives at the left heart insufficiently oxygenated and pollutes the arterial blood; oxygen unsaturation and  $\text{CO}_2$  retention in the systemic blood follows, manifested by dyspnea and cyanosis.

It is obvious that with more complete collapse of the diseased portions of the lung circulation in them will be suppressed and the above disturbances will disappear (Meakins and Davies<sup>110</sup>). This explains the curious phenomenon that collapse of the diseased lung improves respiration and raises the oxygen content in the arterial blood, although it decreases the area of the respiratory field. From the above it becomes clear that slowing down of gas absorption in the pleura is brought about by a double mechanism; thickening of the pleural membrane, and decreased circulation due to the collapse of the lung.

These changes in ventilation and circulation of the collapsed lung explain the changes occurring in the composition of the air of the pneumothorax. As will be shown later, in closed pneumothorax of some duration the percentages of oxygen are lower and of  $\text{CO}_2$  higher than would be expected. The question was raised whether the gaseous content of the pleural cavity in pneumothorax was in equilibrium with the alveolar air, the arterial blood, the venous blood or the "lymphatic air" (S. di Pietro,<sup>118</sup> Webb, Gilbert, James and Havens,<sup>130</sup> Dautrebande and Spuhl,<sup>74</sup> etc.). It cannot be doubted, I believe, that the composition of pneumothorax is regulated by the gases present in the venous blood circulating in the collapsed zone of the lung which is surrounded by the air of the pneumothorax (Rist and Strohl<sup>123</sup>). Therefore  $\text{O}_2$  decreases and  $\text{CO}_2$  increases as the collapse of the lung advances; conversely, opposite changes occur when the lung is allowed to reexpand. I have found however that when the lung has become completely atelectatic and circulation suppressed in it, again  $\text{O}_2$  rises and  $\text{CO}_2$  decreases, probably because the pleural air is brought to an equilibrium with the venous blood circulating under the parietal pleura. Other causes do influence the composition of the pleural air, and among them the more important is the presence of fluid.<sup>71</sup> Therefore gas analysis of pneumothorax may be of considerable assistance, as will be shown later.

It becomes equally obvious that as long as the pleura remains permeable to gases no positive pressures can be maintained in it for over a few hours at the most. Whatever may be the amount of air introduced into the pleura and the positive pressures reached at the time of the refilling, the pressure will, within a short time, again become negative. Therefore the idea of "active compression" of the lung is physiologically groundless and misleading. Frequent refillings with moderate amounts of air will accomplish more in maintaining an even and elevated intrapleural pressure than great amounts introduced at long intervals.

(d) *Variations in the Ability of the Lung to Expand.*—The thoracic cavity represents a box with partly elastic and partly rigid walls, rhythmically expanding and contracting. The lungs contained in it will necessarily be submitted to the

same changes in size, and air will rush in and out. Thus, inside of the lungs the pressure will remain constantly equal to the outside atmospheric pressure, with but very slight variations ( $-1$  mm. Hg. in inspiration,  $+1$  mm. Hg. in expiration). Therefore the variations in the pressures, which measure the corresponding variations in the elastic recoil of the lung tissue, will present very slight inspiratory and expiratory differences, not exceeding 2 or 3 mm. Hg. This being the case, let us study the changes in intrapleural pressures during respiration in the presence of a unilateral closed pneumothorax with pressure slightly below atmospheric. Let us suppose first that the collapsed lung is able to expand in a normal way and that its elasticity and contractility are not destroyed or altered. It is obvious, that although the intrapleural pressures may be different in the two chests, their oscillations around the respective mean pressures during inspiration and expiration will be equal, provided that the expansion of both chests is equal, and the respective lungs perfectly elastic. *In fact, the enlarged chests during inspiration will be readily filled with the expanding lungs and conversely, chest and lung will collapse together during expiration.* Therefore in these cases the mediastinum will remain immobile in the position that it occupied at rest and which was determined by its degree of mobility and the differences in pressures created by the pneumothorax between the two halves of the chest.

It is not the same if the lung has lost its ability to expand and retract readily. This may be due to the obstruction of the respective bronchi or to the impairment of the elasticity of the lungs, or to an antagonistic contraction of the smooth musculature of the bronchi, and especially of the bronchioli. Under such conditions, the intrapleural pressure in the affected hemithorax will become more negative as the lung cannot expand and fill the enlarged chest, and thus the suction action exerted by the enlarging chest upon the lung is not neutralized by the expansion of the latter. It is peculiar that in the voluminous literature on pneumothorax this point has been considered very little, if any; it is, perhaps, for this reason that so many fanciful theories, already mentioned, have been advanced for the explanation of the so-called "paradoxical movements" of the lung, of the mediastinum or of the diaphragm. They have been considered as abnormal and paradoxical only because the rôle of the lungs acting as elastic ballonets regulating the pressure in the pleural cavities, exactly as internal ballonets regulate pressure in the non-rigid dirigibles, has been completely disregarded. The knowledge of this rôle of the lungs renders the mechanism of these paradoxical movements easy to understand and proves that they are in perfect agreement with the elementary laws of aerodynamics. Consequently they cease to be "paradoxical."

(e) *Selective Collapse.*—The fundamental principles laid down above, render easy the comprehension of the mechanism of selective collapse of the diseased areas of the lung under pneumothorax. I cannot agree with the conception that it is due to a more effective "compression" of the diseased than of the healthy portions of the lung. It is difficult to understand that the diseased parts of the lung, which are infiltrated, hard and resistant, can offer less resistance than the eminently collapsible healthy parenchyma. It seems to me reasonable and in



better agreement with the clinical and radiographic findings to consider that this "selective collapse of the lung" already existed before pneumothorax was induced; so what the latter did was only to render it apparent. In fact, the diseased portion of the lung, more often the apex, was already more or less atelectatic and fibrotic; in fact we know that the intrapleural pressure was considerably lower than on the healthy side and it is for that reason that the trachea and

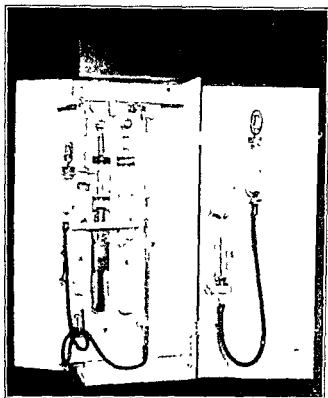


Fig. 7.—Portable gas-analysis apparatus for bedside use. *B*, burette, graduated to 001 c.c. of 10 c.c. total capacity. *C*, tube containing sodium hydroxide, half-saturated solution for absorption of  $\text{CO}_2$ . *O*, tube containing ammonia—ammonium chloride solution and metallic copper, for absorption of  $\text{O}_2$ . *A*, tube containing 1 per cent. solution of sulphuric acid for washing of the burette. *S*, mercury-filled, gas-sampling tube. The panel of the apparatus can slide, thus giving more room for the manipulations. (This apparatus is constructed by Eimer and Amend, New York.) (Coryllos.)

often the heart and the diaphragm were already displaced toward the affected side. After the induction of pneumothorax the trachea, heart and diaphragm return to their normal position although the intrapleural pressure often remains markedly negative. Under these conditions it cannot be reasonably supported that the air has exerted a "selective compression" upon the diseased portion of the lung because the negative value of pressure on the diseased side excludes any idea of compression; furthermore, how is it possible that this "hypothetical" compression had acted "selectively" upon the portion of the lung which, precisely, is the less "compressible"? It is therefore more reasonable to believe that increase of intrapleural pressure has allowed the chest wall to reexpand than

that it has compressed the diseased lung. The student of tuberculosis often wonders how so many unwarranted theories have gained easy and universal recognition and have passed from textbook to textbook without raising any discussion.

From the above it can be concluded that in the study of the mechanics of pneumothorax the condition of the underlying lung, so far neglected, must be given more serious consideration in the future.

### (B) Gas Analysis in Pneumothorax and Its Practical Applications.—

In order to bring gas analysis to clinicians a simple and portable gas-analysis apparatus for  $O_2$  and  $CO_2$  was devised<sup>13</sup> (Fig. 7)\* based on the same fundamental principles as the more accurate but also more cumbersome apparatus in use in laboratories. Accuracy of gas analysis to the first decimal has proved to be sufficient for clinical purposes, so that the lack of greater accuracy (to the second or even the third decimal) is compensated by the ease of manipulation of our apparatus, which permits gas analysis to be made a bedside procedure. This apparatus in its actual form is now routinely used by our residents in the tuberculosis services at the Metropolitan and Seaview Hospitals of the City of New York.

The method consists in taking a sample of air of the pneumothorax before the refilling, by means of a Haldane mercury sampling tube (Fig. 1, S) by means of an ordinary pneumothorax needle following the usual precautions for gas sampling. After this, 100 c.c. of air is introduced in the pleural cavity through the same needle by means of a pneumothorax apparatus; after one minute, a second sample of air is taken. One minute has been found sufficient to establish a good mixture of the 100 c.c. of air introduced with the gases already present in the pleural cavity, and insufficient for any appreciable change in the composition of the mixture by diffusion through the pleural serosa. The refilling of the pneumothorax is then done in the usual way, and the amount of air introduced and the pressures of the pleural air are carefully determined and noted.

The determination of the amounts of  $CO_2$  and  $O_2$  in the two samples is easily accomplished with this apparatus within ten minutes, although for greater accuracy it is advisable to perform two determinations of each sample and take the average of them.

Knowing the values of  $O_2$  and  $CO_2$  in the two samples we can: (1) calculate the amount of air present in the pleural cavity; (2) determine the absorption index of the pleura, and (3) detect the existence of spontaneous pneumothorax.

1. Determination of the amount of air in the pleural cavity. If we designate by  $a$  the per cent. of  $CO_2$  in the first sample (initial air) and by  $b$  the per cent. of the same gas in the second sample (pleural air after the addition of 100 c.c. of air), and by  $x$  the total gaseous content of the pleural cavity, we will have the equation.

$$x \frac{a}{100} = (x + 100) \frac{b}{100} \quad (1)$$

In fact the amount of  $CO_2$  introduced into the pleura with 100 c.c. of air being negligible (0.03 of 1 c.c.), we can consider that the total  $CO_2$  content of the pleural air of the first sample ( $x \frac{a}{100}$ ) is equal to the total  $CO_2$  content of air in the second sample  $(x + 100) \frac{b}{100}$

\* This apparatus is constructed by Eimer and Amend, New York.

Solving the equation for  $X$  we will have:

$$X = \frac{100b}{a-b} \quad (2)$$

which allows by simple calculation to determine the value of  $X$ , that is, the amount of air contained at that time in the pleural cavity. By adding to that amount the amount of air introduced during the refilling, we know the total amount of air left in the pleural cavity at the end of the refilling.

2. The same determination is carried out during each of the following refillings. In this way it is easy to determine with accuracy the index absorption of the pleura, and to establish a curve which will inform us directly of its variations and indirectly of the histological changes in the pleura.

Decrease of pleural capacity because of the development of adhesions, the presence of several air-pouches and the existence or nonexistence of communications between them can easily be detected by this procedure. Furthermore, an accurate study of the changes in the absorbing capacity of the pleura after an oleothorax has been rendered possible by this procedure.

The determination of  $O_2$  in the two samples permits us to check the accuracy of the  $CO_2$  findings.

In fact, by introducing 100 c.c. of air into the pleural cavity, we have added 21 c.c. of  $O_2$  to the previous  $O_2$  content of the pleura. If we designate by  $x$  the percentage of  $O_2$  in the first sample, and by  $x'$  the percentage of  $O_2$  in the second sample, we have the equation:

$$\frac{x}{100} \times 21 = \frac{x'}{100} (x + 100)$$

and solving the equation for  $x' = \frac{21x}{x + 100}$  in which  $x$  and  $x'$  are already known.

In this way if the calculated amount of  $x'$  is equal to the  $x'$  given by the analysis of the second sample, the previous determination of  $a$ ,  $b$ , and  $x$  are correct.

For avoiding calculations, tables and curves have been compiled which give at a glance the values of  $x$  and  $x'$  corresponding to  $a$ ,  $b$  and  $x$  found by the analysis.

3. Diagnosis of spontaneous pneumothorax and its course. The following example will show the degree of variations in the values of  $O_2$  and  $CO_2$  in spontaneous pneumothorax, and the information given by them:

V. C. WHITE, female, 36 years. Had spontaneous pneumothorax 2 weeks previously. Admitted to Metropolitan Hospital August 18, 1931, with tuberculosis of left lung, caseous pneumonic form; left pneumothorax and oleothorax were present, with left lung almost completely collapsed; fluid present; shifting of mediastinum to right side. Gas analysis gave following results:

(a) August 21, 1931:	$CO_2$ ....	62
	$O_2$ .....	42
(b) August 25, 1931:	$CO_2$ ....	11.5
	$O_2$ .....	13
(c) September 16, 1931:	$CO_2$ ....	14.0
	$O_2$ ....	07, large amount of fluid
(d) September 17, 1931:	$CO_2$ .....	13.6
	$O_2$ .....	2.1
(e) September 25, 1931:	$CO_2$ .....	11.9
	$O_2$ .....	80

In (a) the pleuropulmonary fistula was still open. In (b) and (c) it remained closed; the rise in the  $O_2$  content in (d) indicated that it opened again, although no clinical symptoms were present at that time. Our diagnosis of a new attack of spontaneous pneumothorax was soon corroborated by the appearance of clinical symptoms, elevation of temperature, dyspnoea, cyanosis, rise of intrapleural pressure and expectoration of Gomenol oil. Gas analysis in (e) showed that the  $O_2$  rose to 80 per cent.

The diagnostic significance of gas analysis is important in cases of unusually prolonged air retention in the pleura after artificial pneumothorax, followed or not by spontaneous pneumothorax. With our usual means of investigation it is often impossible to differentiate with any degree of accuracy whether there is loss of absorbing capacity of the pleural serosa or persistence of a pleuropulmonary communication small enough not to be disclosed by clinical signs. Gas analysis of the content of these air pouches gives a definite answer to this problem. The following case illustrates this point:

J T, white, male, 20 years of age. Admitted to Metropolitan Hospital on January 31, 1929, for tuberculosis of left lung, caseous pneumonic type. Pneumothorax was induced on February 2, 1929, and refillings repeated regularly until July 25, 1929, when spontaneous pneumothorax had occurred, rapidly accompanied by fluid. Fluid was removed repeatedly, replaced by equal volume of air. Patient had improved and was sent to Otisville Sanatorium. Patient readmitted on March 2, 1931; in September pneumothorax was unchanged, although no further refillings were given. In order to determine whether the pleuropulmonary fistula was still open or the pleura had become impermeable to gases, a gas analysis was made, which gave  $\text{CO}_2$  8.5 per cent, and  $\text{O}_2$  1.8 per cent, showing that the fistula was closed.

The reasons for the relatively low values of  $\text{O}_2$  and high values of  $\text{CO}_2$  are actually under investigation; it appears so far that the principal cause is the presence in the pleural cavity of the collapsed lung; the alveolar blood circulating in the collapsed, but not atelectatic peripheral zone of the organ, passes through ill-aerated channels, so that it contains more  $\text{CO}_2$  and less  $\text{O}_2$  than normally. However, the presence of innumerable white cells in the fluid, which consume  $\text{O}_2$  and give up  $\text{CO}_2$  and the action of lactic acid upon the bicarbonates of the exudate seem to contribute to this discrepancy, as shown by the following experiment: In a sampling mercury tube pus from a pyo-pneumothorax was taken (7 c.c.), the tube was filled with pure  $\text{O}_2$  and was allowed to remain in the incubator for 24 hours. Analysis of the gas in the tube showed that  $\text{CO}_2$  was present in a proportion of 5.0 per cent. In two other specimens of the same fluid the tubes were filled respectively with nitrogen and helium instead of  $\text{O}_2$ . Again, after a 24 hour stay of the tubes in the incubator 5 per cent. of  $\text{CO}_2$  was found in the neutral gases while the  $\text{O}_2$  content of the fluid had greatly diminished.

From the above it appears that gas analysis of the gaseous content of pneumothorax is a procedure which can give us valuable clinical information. Since Davy, over 100 years ago (1823), injected air into the pleural cavity of animals for the purpose of studying the quantitative changes occurring in them, several investigators have been interested in this question. Sackur<sup>124</sup> and Harley<sup>89</sup> and lately Martini and Heymer<sup>109a</sup> investigated the influence of lung compression by artificial pneumothorax upon gas exchanges in pulmonary tuberculosis. Henderson and Haggard<sup>94</sup> have studied the absorption of gases injected into the peritoneum, and Laconte and Demarquay,<sup>104</sup> Campbell<sup>60, 61</sup> and others, the absorption of gases injected under the skin. Birnbaum and I<sup>68</sup> have more recently investigated the absorption of gases and vapors ( $\text{O}_2$ ,  $\text{H}_2$ ,  $\text{N}_2$ ,  $\text{CO}_2$ , nitrous oxide, ether, ethyl chloride, ethylene, helium, etc.) by the lung previously rendered atelectatic and by the pleura of dogs and rabbits.

**Physiology of Thoracoplasty.**—The treatment of pulmonary tuberculosis by thoracoplastic collapse of the tuberculous lung is conditioned by the same

mechanical and biological principles as the treatment by bed rest or by pneumothorax.

The removal of a part of the bony skeleton of the chest deprives that portion of the rigidity which rendered it able to resist the atmospheric pressure. Thus the deribbed chest yields and the underlying portion of the lung, not being forced to expand, remains collapsed. This brings about collapse and closure of the small bronchioli and gradual absorption of the air entrapped in the alveoli. Collapse of the lung is thus gradually transformed into atelectasis which leads to circulatory deficiency and fibrosis. The latter is especially marked in the diseased area of the lung as has been shown above. This succession of events, collapse of the lung, atelectasis and fibrosis explains the progressive improvement of the tuberculous lesions following thoracoplasty; on the other hand the definite collapse of the alveoli and their fibrotic organization prepare the ground for the development of bronchiectasis which is a frequent complication in the collapsed lung. It is my contention that in tuberculosis as in any other pulmonary disease, atelectasis and prolonged infection leading to definite closure of the alveoli are the intermediate and necessary anatomical conditions between pulmonary diseases and bronchiectasis.

Besides collapse and atelectasis of the lung, thoracoplasty produces a definite immobilization of the chest, due to development of bony tissue on the partially resected periosteum and formation of bony bridges between stumps of the resected ribs. This immobilization is limited to the portion of the chest operated upon; in fact in partial thoracoplastic operations which are limited to the upper portion of the chest, for apical lesions, the lower part of the hemithorax conserves a degree of mobility sufficient to allow an almost normal function of the lower lobe. This selective collapse is one of the advantages of thoracoplasty over pneumothorax.

A question to be elucidated is whether thoracoplasty produces "compression" of the corresponding portion of the lung or simply acts by producing only definite collapse of the lung. The significance of this point is not merely academical; it has an important bearing upon the technique of the operation.

The solution of this problem requires a careful consideration of the physio-mechanical factors involved, that is, of the pressures exerted upon the normal chest and of the changes in these pressures following thoracoplasty. Obviously the pressure exerted upon the chest wall is equal to the difference of pressures exerted upon its external and internal surfaces. The first is equal to one atmosphere, namely 760 mm. Hg. The second is equal to one atmosphere minus the value of the mean negative intrapleural pressure, that is about  $-7$  mm. Hg. ( $760 - 7 = 753$  mm. Hg.). Thus the pressure exerted upon the chest is equal to  $+7$  mm. Hg. which roughly is  $1/100$  of the atmospheric pressures. In other words, if we assume that the average external area of the hemithorax equals 250 square inches, the pressure exerted upon it is equal to 30 pounds in round figures. This pressure is supported by the chest because of the presence of the bony skeleton in the chest wall; therefore, when the ribs are resected this pressure will act upon the deribbed soft wall and will push it inwards. From that, it was rather hastily concluded, that the underlying lung was compressed by the collapsed chest wall.

It does not seem to me that this conclusion is justified. A close study of the positive pressure exerted upon the chest showed that this is a function of the intrapleural negative pressure; so that they always remain equal and of different sign. In order to make clear this statement, let us suppose that before thoracoplasty the negative intrapleural pressure was  $-7$ ; obviously the positive

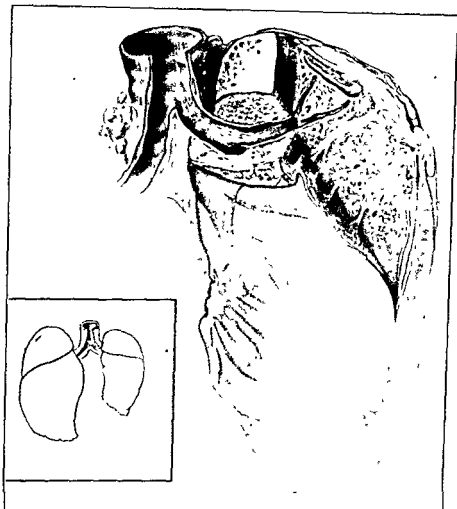


Fig. 8.—M. S., W. F., 23. Large tuberculous cavity in left apex—following thoracoplasty (6 ribs) cavity was closed and sputum became negative. Death 7 months later from another cause. Postmortem showed that cavity was closed and bronchus leading to the cavity was obliterated.

pressure exerted upon the external surface of the chest was  $+7$  mm. Hg. As the chest wall collapses the intrapleural pressure increases to  $-6$ ,  $-5$ ,  $-3$  and finally to 0; in parallel manner the positive pressure decreases to  $+6$ ,  $+5$ ,  $+3$  and finally to 0. Thus when the chest is completely collapsed further "push" from the outside ceases. Therefore there cannot be any question of "compression" in thoracoplasty any more than in pneumothorax when the pleura is still permeable to gases. That closure of cavities is caused by obstruction of the communicating bronchi, is shown by the following two cases. In the first (Fig. 8),

a thoracoplasty produced closure of the cavity. The patient died from an unrelated cause. The autopsy specimen showed that the bronchus leading to the collapsed cavity was completely obstructed. In the second case (Fig. 9), thoracoplasty did not close the cavity. Autopsy specimen showed that the bronchus leading to the cavity was still patent.

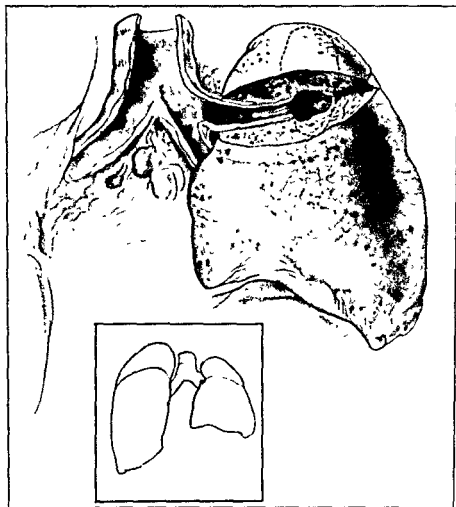


Fig. 9.—A. S. W. M., 42. Huge tuberculous cavity in left apex. Extensive thoracoplasty (9 ribs) followed by revision and entrapleural packing 4 months later failed to collapse the cavity. Postmortem showed a large draining bronchus had remained patent.

*Conclusions.*—From the above considerations we can draw a number of conclusions of practical importance. *First*, that the longest segments possible of the ribs should be resected in order to insure a sufficient collapse of the chest. *Second*, that in dealing with cavities situated posteriorly and internally it is necessary to remove also the posterior segments of the ribs, and even portions of the transverse apophyses. *Third*, that in a number of cases with extensive lesions no satisfactory collapse can be obtained without resection of the ribs in their entire length and often of their cartilages. And last, that in cases with

pleural exudate or pneumothorax it is necessary to empty the fluid or the air or both before thoracoplasty; otherwise the collapse of the chest wall will be incomplete because after the chest has become immobilized by the development of new bone, which generally occurs within the fourth or fifth week after operation, subsequent absorption of air or exudate will allow partial reëxpansion of the underlying lung. Thus a complete collapse at the time of the operation may become incomplete after a while and allow the reopening of cavities which were temporarily closed.

The biological mechanism of cure of tuberculosis following thoracoplastic collapse of the diseased lung is thus exactly the same as in collapse by artificial pneumothorax or in prolonged bed rest.

There is, however, one fundamental difference between the physiological action of pneumothorax and of thoracoplasty. In the first the degree of collapse varies with the absorption of air. It is at its maximum immediately after each refill and at its minimum before it. On the contrary, following thoracoplasty, collapse of the lung is at its maximum and will remain unchanged. It was shown above that fibrosis develops when the tissues were deprived of their circulation and this anoxemia has persisted for a length of time. In the example of ischemic paralysis of Volkmann given above, fibrous degeneration of vessels does not occur if a tight bandage is applied only intermittently upon the arm, even if the total duration of its application exceeds the time of application of a permanent tight splint. In pneumothorax, pulmonary collapse is intermittent because the lung is allowed to reëxpand between refills and, therefore, circulation is reëstablished in it. On the contrary, in thoracoplasty, collapse and ischemia are permanent and definite. This conception offers an explanation to the well-known fact that pneumothorax becomes more efficient as the pleura becomes thicker, more resistant and less permeable to gases and consequently refills less frequent. For the same reason development of fluid in the pleural cavity very often leads to closure of cavities which have resisted an uncomplicated pneumothorax.

The above considerations on the pathologic physiology of the tuberculous lung have opened new horizons to the phthisiologist and the thoracic surgeon and have placed at their disposal a new method of investigation. This study has only begun. I feel convinced that further investigation in this direction will be of help in our efforts to check this disease and save human lives.

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## **SECTION B.**

**(Chapters VI to XI.)**

## **DIAGNOSIS.**

**Laboratory, Physical, Symptomatic.**

**Classification: X-ray, and Differential  
Diagnosis of Pulmonary Tuberculosis.**

## CHAPTER VI.

# DIAGNOSIS OF TUBERCULOSIS BY LABORATORY TESTS.

K. ROBERT KOCH AND RALPH R. MELLON

**Laboratory Diagnosis.**—During the last decade considerable progress has been made in the laboratory diagnosis of tuberculosis through the development of practical methods for the cultivation of tubercle bacilli directly from infected material. However, it would be misleading to accept the contention of some authors that this method has been advanced to such a degree that it could replace animal inoculation. Direct smear examination, especially of sputum, still remains a procedure indispensable for routine examination. The findings in one good specimen of sputum are of more significance than the examination of a series of poorly collected specimens. Every examination should be started with a study of a direct smear prepared from a selected particle of sputum. Decolorizing is difficult unless the smears are prepared thin and even. The number of staining methods for tuberculosis is very large. Comparative tests, however, have demonstrated that the Ziehl-Neelsen method with or without minor modifications remains the most suitable technic. Pinner<sup>27</sup> reported lately that in his experience the Cooper<sup>2</sup> modification seemed to have some definite advantages without complicating the procedure.

**Staining Methods for the Tubercle Bacillus.**—Flood the slide with fresh carbol-fuchsin to which 3 c.c. of 10 per cent. sodium chloride per 100 c.c. is added; steam for four minutes and allow to cool until the precipitate forms. Wash with tap water. Decolorize with acid alcohol (5 c.c. nitric acid, sp. gr. 1.42 plus 95 c.c. of 95 per cent. alcohol), wash, two minutes 95 per cent. alcohol; wash, counterstain with 1 per cent. brilliant green in 1:10,000 sodium hydroxide for one minute; wash, dry. (*Pinner recommends 2.5 to 3 per cent. hydrochloric acid in 95 per cent. alcohol as a more satisfactory decolorizing agent because traces of nitrous acid may decolorize tubercle bacilli.*)

Examination for elastic fibers should be carried out in the unstained preparation. Jessen<sup>14</sup> described a staining method for staining both tubercle bacilli and elastic fibers in the same preparation.

**Method.**—Use the Ziehl-Neelsen stain and counterstain for one or two minutes with:

Hematoxylin .....	1.0 Gm.
Lithium carbonate, saturated solution.. . . .	1.0 c.c.
Absolute alcohol .....	200 c.c.
Distilled water .....	200 c.c.

Then rinse, cover for a few seconds with 28 per cent. ferric chloride, rinse, dry.

Although Much's nonacid-fast granules cannot be accepted as diagnostic criteria at the present time, a method for their demonstration has been given by Kiefer.<sup>15</sup>

#### Kiefer's Stain:

Carbolfuchsin, 4 parts; carbol methylviolet, 3 parts—by volume.

If this mixture shows a metallic scum, add 95 per cent. alcohol drop by drop until the scum disappears.

#### Fixing solution:

Iodine .....	1 Gm.
Potassium iodide .....	2 Gm
Distilled water .....	100 c.c.

#### Decolorizing solution:

Concentrated hydrochloric acid . . . . .	10 c.c.
Alcohol, 95% .....	50 c.c.
Acetone .....	40 c.c.

#### Counterstain:

1 per cent. aqueous methylene blue.

Stain while heating  $\frac{1}{2}$  to  $\frac{3}{4}$  minute, rinse; iodine solution 1 to  $1\frac{1}{2}$  minutes, rinse; decolorize  $\frac{3}{4}$  to 1 minute, rinse; counterstain.

It is obvious that the composition of the nonacid-fast flora of the sputum can be surveyed better in a direct smear than by attempts to cultivate these organisms.

When examinations of direct smears fail to demonstrate tubercle bacilli, specimens should be subjected to further study by a concentration method. Corper has estimated that more than a hundred thousand bacilli must be present in 1 c.c. of sputum for their detection in smear preparations. Of the concentration methods two are most widely used: the anti-formin method and Petroff's<sup>25</sup> homogenization by alkalis. Where those methods also fail, culture or animal inoculation should be resorted to, also in every case where it is desirable to determine the type of tubercle bacillus.

### ANIMAL INOCULATION.

All methods designated to hasten the development of tuberculous lesions in animals have not attained their purpose. The best way of injection is still the subcutaneous route in the region of the groin of two guinea-pigs with the concentrated sediment of a specimen neutralized and resuspended in 1 to 2 c.c. of normal saline. Guinea-pigs used for inoculation need not be tested with tuberculin before infection because spontaneous tuberculosis in animals kept under sanitary conditions is rare and can be easily distinguished from an inoculation tuberculosis. The latter must show a primary lesion and a spread of the infection unilaterally by the way of the regional lymph nodes. Intracutaneous tuberculin tests may be done starting approximately two weeks after the infection but even an animal exhibiting a positive tuberculin reaction should not be discarded without autopsy. Animals should be kept for 4 to 6 months.



It has been the general opinion that guinea-pigs are the most susceptible reagents to living tubercle bacillus. A single bacillus was supposed to be sufficient to lead to a fatal outcome. However, such a statement leaves out of consideration the fact that in any animal experiment we are dealing with several factors influencing the outcome of the test: (a) Variation in the virulence of the organism. (b) Variations in the individual resistance of the animal. (c) Susceptibility of the infected animal to other infection. (d) Insusceptibility of guinea-pigs to the avian tubercle bacillus.

Animals dying within 3 weeks after infection and lacking macroscopic tuberculous lesions require microscopic examination.

### CULTIVATION OF TUBERCLE BACILLI.

The *cultural method* plays a significant part in the demonstration of tuberculosis. While it has not replaced the animal test it has definite advantages under certain conditions which make it a very helpful test. The two factors which influence the results are: (a) a suitable method for the exclusion of other bacteria, and (b) suitable culture media. In order to exclude nonacid-fast organisms in specimens the material may be treated with either alkali or acid in a concentration which kills organisms without injuring the viability of the tubercle bacillus. Acid-fast saprophytic bacilli are more susceptible to the action of acids and alkalis than the tubercle bacillus and can be destroyed by such preliminary treatment. The high non-saponifiable fraction of lipoids (tubercle bacillus contains 60 to 70 per cent. of the total lipins as non-saponifiable lipoids while saprophytic acid-fast bacilli show values of 4.5 to 5 per cent. Long and Campbell<sup>20</sup>) may account for the protection of tubercle bacilli against acids and alkalis. For practical purposes the consistency of the specimen and the number of contaminating bacteria present should be taken into consideration when estimating the concentration of acids for preliminary treatment. It may be completely discarded when a routine culture proves the specimen to be free of organisms growing on ordinary media.

### PETROFF'S METHOD.<sup>25</sup>

Equal parts of the material and 4 per cent. sodium hydroxide are well mixed and incubated from 15 to 20 minutes at 37° C. in centrifuge tubes. (Sweany and Evanhoff and Pinner prefer to use a 3 per cent. sodium hydroxide solution.) In order to insure uniform mixture it should be shaken every 5 to 10 minutes. It is then centrifuged at high speed for 10 minutes. The supernatant fluid is then decanted very carefully and to the sediment from 1 to 2 drops of normal hydrochloric acid are added. The amount of hydrochloric acid necessary depends upon the amount of sediment in the tube. This sediment is then planted on gentian violet egg tubes or other media.

**Preliminary Treatment with Acids.**—Hydrochloric or sulphuric acid (Sumiyoshi,<sup>20</sup> Loewenstein<sup>18</sup>; modified by Hohn<sup>12</sup>): The material is mixed with equal parts of 10 per cent. (volume) hydrochloric acid or sulphuric acid and left at room temperature for 30 minutes with occasional shaking. It is then centrifuged for 10 minutes at high speed, the supernatant fluid decanted and

the unwashed sediment is spread over the surface of the culture tubes. Corper recommended adding equal parts of 6 per cent. oxalic acid. The specimen is then diluted with the sterile saline and incubated for 30 minutes. A number of authors prefer not to use a fixed concentration but vary the concentration from 6 to 12 per cent. according to the contaminations of the specimens.

The following table illustrates clearly the effect of various concentrations of sulphuric acid upon the viability of tubercle bacilli and other nonacid-fast organisms. The lower the concentration of acid, the better the tubercle bacilli grow; however, in the lowest concentration the growth of contaminating organisms is so abundant that it impairs the purpose of the method. One c.c. of sputum was added to 5 parts sulphuric acid, 30 minutes contact, and centrifuged for 10 minutes, no neutralization.

MEDIUM LUBENAU, 6 TUBES FOR EACH CONCENTRATION

Time required for appearance of growth Days	Percentage of tubes showing growth in varying concentrations of H <sub>2</sub> SO <sub>4</sub>				
	3%	5%	7%	10%	15%
7	0	0	0	0	0
10	45 5%	23.1%	14 3%	0	0
14	63 6%	61 5%	50.0%	35 7%	23.7%
21	81 8%	92 3%	71 4%	50 0%	30.8%
35.	81 8%	100 0%	85 7%	71 4%	61.5%
Contaminations	31 8%	14 1%	10 7%	4 8%	1.3%

Spores contained in specimens such as stools cannot be destroyed by preliminary treatment with acids or alkalis, but their germination may be prevented by the addition of malachite green or brilliant green (1 to 4000 concentration) to the culture medium. It may be mentioned here that acid metabolism products of organisms may change part of the monobasic salt of the dye into the dibasic which is deep bluish green while alkaline products tend to set free the dibase (carbonal base) which is almost colorless. Sodium hydroxide destroys a number of organisms other than acid-fast present in the material, but is more effective for Gram-negative than for Gram-positive bacteria. Gentian violet on the other hand inhibits the growth of most Gram-positive bacteria. The selection of a method for preliminary treatment depends somewhat upon the culture media used for inoculation. The alkaline treatment has the disadvantage of requiring neutralization. Aside from the time consumed by this procedure the possibility of contamination is increased.

#### SUITABLE MEDIA FOR CULTIVATION.

1. *Lubenau's*<sup>21</sup> *Egg Medium*—Three parts of well mixed whole eggs are added to one part of 5 per cent. glycerol nutrient broth. This mixture is tubed and inspissated for 2 or 3 hours at 90° C. *Hohn*<sup>12</sup> emphasized the necessity of adding a small amount of glycerol broth to each tube. He further recommended that some hemoglobin be added to the medium, in the following way:

6. *Petragnani's*<sup>24</sup> *Medium*:

Milk .....	900 c.c.
Potato flour .....	36 Gm
Peptone .....	6 Gm.
Potato (egg size pieces) .....	6

This mixture is kept in a boiling water bath with frequent stirring until it becomes sticky; after this it is left in the water bath for from one to two hours. After cooling to 50° C, 24 whole eggs and 6 egg yolks, 70 c.c. of glycerol, and 50 c.c. of a 2 per cent. aqueous solution of malachite green are added; the whole mixture is filtered through sterile gauze, tubed, and solidified in the same way as the preceding medium.

These media are kept in the incubator for not less than three days before use.

7. *Egg yolk agar media* (*Herrold*<sup>11</sup>).

Liebig beef extract .....	3 Gm.
Peptone . . . . .	10 Gm.
NaCl .....	5 Gm.
Agar .....	10 Gm.
Distilled water .....	1000 c.c.

The mixture is adjusted to approximately pH 7.5. The yolk of one egg is added to 150 c.c. of melted agar at a temperature of 60° C. The agar is allowed to cool to about 40° C and tubed or poured into petri dishes.

The earliest colonies may appear within 5 to 10 days. Most inoculations, however, require 10 to 40 days incubation. No tube should be discarded before 60 days observation. All slants should be examined by smear preparation even if visible typical or atypical colonies are absent. Colonies are more easily visible on a medium containing dye than on a plain medium. It has been reported repeatedly that scrapings from apparently sterile slants contain occasionally acid fast rods. Transfers from such slants to a new medium are practically always negative and animal inoculation of the surface washings fails to produce lesions in such instances. At the present time it remains a matter of doubt whether we are dealing with true tubercle bacilli in such cases. The culture method opens up the possibility of studying the appearance of atypical tubercle bacilli and their relation to the clinical course of the disease in a way which has not been possible so far.

The chart<sup>31</sup> on page 9 gives comparative results of the cultivation of fourteen specimens of sputum on different culture media. Each specimen was inoculated into 6 tubes of the respective media; 84 tubes altogether. Preliminary treatment: 5 per cent. sulphuric acid; 5 parts to 1 c.c. of sputum; 30 minutes contact.

The efficiency of the media for growing tubercle bacillus and the number of contaminations in the various media show a close parallelism. Loewenstein's and Petragnani's media gave the best results. Colonies on Hohn's medium developed as fast as on the other two media, but the total number of positive cultures was less and the number of contaminated tubes higher.

Beside the solid type of medium, liquid media have also been used for diagnostic purposes although they have not been studied as intensively. The

NUMBER OF TUBES SHOWING GROWTH ON FOLLOWING MEDIA

Period of growth Days	Petroff	Petragnani	Hohn	Loewenstein	Herrold	Lubenau
5	0	1	0	1	0	0
7	0	8	3	9	1	0
10	8	18	27	31	3	2
13	32	52	49	72	32	21
15	37	66	49	76	42	30
21	58	76	63	83	53	56
35	66	76	64	83	57	57
Contaminated	3	0	7	0	16	10

results reported so far do not seem to be inferior to those obtained on solid media.

Liquid media suitable for the cultivation of tubercle bacillus:

#### 1. *Besredka-Wolters*<sup>24</sup> Broth.

The yellow of two eggs is shaken with glass pearls and mixed with 100 c.c. of distilled water. One per cent. sodium carbonate solution is added slowly until the mixture becomes transparent (approximately from 2 to 4 c.c. to 10 c.c. media). Add distilled water up to 700 c.c., tube and sterilize. Add 7.5 c.c. of a 2 per cent. malachite green solution.

#### 2. *Kirchner*<sup>16</sup> Medium.

(a) Disodium phosphate . . . . .	3 Gm
Monopotassium phosphate . . . . .	4 Gm.
Magnesium sulphate . . . . .	0.6 Gm
Sodium citrate . . . . .	2.5 Gm
Aqua dest. . . . .	1000 c.c.
(b) Salts the same	
0.5% asparagin but no glycerine	
(c) Disodium phosphate . . . . .	3 Gm.
Monopotassium phosphate . . . . .	4 Gm
Magnesium sulphate . . . . .	0.6 Gm
Sodium citrate . . . . .	2.5 Gm.
Asparagin . . . . .	5 Gm.
Glycerine . . . . .	20 Gm.
Aqua dest. . . . .	1000 c.c.

The medium is kept ready sterilized in flasks, when needed 10 per cent. serum is added, the medium is tubed in quantities of 6 c.c. and incubated for 48 hours for sterility tests. The media are clear and without sediments.

While the growth of the tubercle bacillus on the surface serves primarily for the preparation of tuberculins or the cultivation of large quantities of tubercle bacilli for analytical studies, the culture of tubercle bacilli in the depth of the liquid medium is suitable for examination of infected material. Growth appears in the bottom of the tube in the form of small granules, which with age become larger. The supernatant fluid thus remains clear, making it easy to differentiate the tubercle bacillus culture from the growth of other organisms. A disadvantage of the deep liquid culture is that the sediment obtained from acid treated material

for inoculation resembles tubercle bacillus growth so much in the early stages that macroscopic differentiation is impossible. Careful daily observation gives an approximate idea of the increase of the granules in volume.

*Results.*—The results recorded in the following table were obtained from material treated with sulphuric acid where contaminations were present. The acid material was inoculated without washing on Lubenau medium and into Kirchner liquid medium.

TABLE I

	Positive	Media		
		Lubenau & Kirchner	Lubenau only	Kirchner only
Sputum . . . . .	34	19	11	4
Urine . . . . .	4	4	....	....
Spinal fluid . . . . .	6	4	....	2
Pleura exudate . . . . .	3	2	....	1
Material from gland puncture . . . . .	18	4	9	5
Pus from abscesses . . . . .	14	7	6	....
Stomach content . . . . .	7	1	5	1
Total . . . . .	86	41	31	13
Contaminated . . . . .	....	....	5	1

The following table by Wolters and Dehmel in which results on Petragnani, Besredka and Besredka-Wolters media are compared, demonstrates the value of malachite green as an inhibitory factor for the growth of contaminating bacteria. Material, sputa. Preliminary treatment, 15 per cent. hydrochloric acid.

TABLE II

Type of Medium	No of specimens examined	Culture positive	Culture negative	Contaminated
Petragnani . . . . .	310			4
	Smear, positive 55	52	3	....
	Smear, negative 255	12	243	....
Besredka . . . . .	205			26
	Smear, positive 32	32	0	....
	Smear, negative 173	5	168	....
Besredka-Wolters . . . . .	149			0
	Smear, positive 30	25	5	....
	Smear, negative 119	3	116	....

**Corper's Substrate Culture Medium.**—Place 1 c.c. of finely divided material in sterile test-tubes with sterilized cork, add 0.5 c.c. sterile citrated blood ( $\frac{1}{10}$  volume of sterile 3 per cent. neutral dry sodium citrate) or fresh egg yolk. Mix well and add  $1\frac{1}{2}$  to 2 volumes of 6 per cent. sulphuric acid or 3 per cent. hydrochloric acid and mix again by shaking. Place in incubator at 37° C. for  $\frac{1}{2}$  to 1 hour with repeated vigorous shaking. Remove and neutralize with 1.3 per cent. sodium carbonate containing 3 per cent. glycerine, using bromthymol blue as indicated. Allow settling of sediment over night in refrigerator. Decant super-

natant fluid carefully, leaving 2 to 3 c.c. behind. After breaking up the sediment by shaking, the tube is carefully stoppered and placed in a dark incubator at 37° C. Smears are prepared weekly and stained by Ziehl-Neelsen's technic.

TABLE III

	Positive cultures in				Total positive
	2 weeks	3 weeks	6 weeks	12 weeks	
Tissue substrate method					
Sputum and blood	1	21	17	4	43
Sputum and yolk	0	19	15	4	38
Oxalic acid. Potato medium	1	7	36	7	51

According to Corper the tissue substrate culture should find easy adaptability for the practitioner and fill a place as a simple, delicate diagnostic procedure. This method has not been tested by others. It has the distinct advantage of not requiring storing of media and may therefore become a very useful method, not so much for the practitioner but for the small laboratory which cultures tubercle bacilli only infrequently.

*Conclusion.*—From the data available the conclusion is justified that the culture method is superior to smear examination. A requisite for the successful application of the method is a constant supply of fresh media and the inoculation of several tubes of at least two different media. Laboratories, which only occasionally attempt to demonstrate tuberculosis by culture, should rely upon the animal test or try Corper's substrate method. In cases where the demonstration of tubercle bacilli by the laboratory is the deciding factor for the diagnosis of a patient, both animal inoculation and the culture method should be carried out, because statistical data of extended observations do not support the claim of the superiority of the culture method. Only once in a while positive cultures are secured from specimens which did not lead to a tuberculous process in animals. In the examination of 105 specimens we obtained positive cultures from four in which the guinea-pigs failed to develop tuberculosis, on the other hand, 11 guinea-pigs were positive, where the culture method failed. The advantage of the culture method is greater speed of diagnosis. The following tables compiled by Pinner illustrate these points very well:

TABLE IV

A COMPARISON OF CULTURE AND GUINEA-PIG INOCULATIONS IN 92 SPECIMENS FROM TUBERCULOUS PATIENTS

(Including sputum, feces, exudates, tissues, urine, all negative on direct smear)

Number of Specimens	Positive on culture (Per Cent.)	Positive on animal inoculation (%)	Culture Positive; Guinea-Pig Negative	Guinea-Pig Positive Culture Negative	Positive by any one method (%)
37	78.3	89.1	4	8	100.0
55	65.4	96.3	2	19	100.0

TABLE V

A COMPARISON OF CULTURE AND GUINEA-PIG INOCULATION  
IN 238 MISCELLANEOUS SPECIMENS

(Including sputum, urine, exudates, tissues, all negative on direct smears)

Number of Specimens (Negative on direct smear)	Positive After Concentration	Positive on Culture	Positive on Animal Inoculation	Positive by any one method	Culture Positive; Guinea-Pig Negative	Guinea-Pig Positive; Culture Negative
238	9	39	52	56	4	17

TABLE VI

A COMPARISON OF CULTURE AND GUINEA-PIG INOCULATION IN  
REGARD TO THE SPEED OF DIAGNOSIS

(Accumulative percentages of positive diagnosis obtained in 10 day periods)

Days	10	11-20	21-30	31-40	41-50	51-60
Culture.	77	33.3	71.7	81.9	89.6	97.3
Guinea-Pig		0	30.7	63.4	86.5	94.3

**Blood Cultures.**—Of particular interest are Loewenstein's reports<sup>10</sup> of the successful cultivation of tubercle bacilli from the blood stream. He uses the following technic.

**Technic.**—Five to 10 c.c. of blood are taken under sterile conditions into 3 c.c. 10 per cent. sodium citrate solution. Sterile distilled water is added to 50 c.c. The tubes are centrifuged and the sediment shaken for 5 minutes with an equal amount of 15 per cent. sulphuric acid, sterile water is added again to 50 c.c. after centrifugation. The supernatant fluid is decanted and washed once more with sterile distilled water. After centrifuging the sediment is transferred to the asparagin egg medium by means of capillary pipettes.

The culture method proved in the hands of Loewenstein, superior to animal inoculation. Positive cultures when inoculated into guinea-pigs showed variations in virulence, some animals developing tuberculous lesions only as late as 12 to 15 months after inoculation. The diagnostic value of the method is impaired not only by the fact that only a small number of investigators have been able to confirm Loewenstein's results, while the majority failed completely; but also by the fact that Loewenstein himself obtained positive cultures from patients with diseases not ordinarily etiologically associated with tuberculosis, such as acute polyarthritis, chorea, multiple sclerosis, and dementia præcox. In some of the patients, from which Loewenstein obtained tubercle bacilli blood cultures during life, autopsies failed to reveal macroscopic and microscopic tuberculous lesions. The demonstration of tubercle bacilli in the blood of a patient either with well characterized or with indefinite symptoms does therefore not justify the conclusion of a causative relationship. Yet some of the laboratory findings still require an explanation. In acute rheumatic polyarthritis, for example, clinical evidence registers a coincidence with an active tuberculous process in less than 1 per cent. of the patients, but it appears remarkable that this

group of patients gives a complement fixation with tuberculous antigen in a high percentage. These serological reactions cannot be dismissed as entirely non-specific. A clue to an explanation may be found in the reports by Boquet, Negre, Freund, Krah and Witebsky,<sup>1, 33</sup> who observed that diphtheria bacilli and diphtheroids as well as tubercle bacilli, absorbed the antibodies from tuberculous serum. The antibodies, with which the arthritic patient reacts with tuberculous antigens, may well be diphtheroid antibodies, the diphtheroids being dissociated from the tubercle bacillus itself (see chapter on Variation).

### DIFFERENTIATION OF HUMAN, BOVINE AND AVIAN TUBERCLE BACILLI.

As long as animal inoculation was the only means for differentiating the various types of tubercle bacilli, its practical application remained limited. Attempts to establish a type diagnosis by morphological differences of the bacilli, by determination of the acid or alkaline formation or by serological tests failed. The cultivation of tuberculous infected material which permits the observation of the morphological characteristics of the tubercle bacillus colonies, has made it possible in most cases to determine the type even in routine examinations, when such information seems desirable.

According to Griffith,<sup>9</sup> cultures may be separated into those exhibiting:

1 Eugonic (luxuriant) growth and pigment formation; such strains can be diagnosed as human type without animal inoculation.

2 (a) Dysgonic (scant) growth and pigment formation: human type, not pathogenic for rabbits, pathogenic for guinea-pigs (rare).

(b) Dysgonic growth, no pigment formation: bovine type, pathogenic for rabbits and guinea-pigs

Several points have to be observed for a definite *type differentiation*. The test should be carried out with freshly isolated or little subcultured strains and young and actively growing cultures (not older than 14 days) should be used for culture and animal inoculation. In the selection of media the glycerol content must be considered. A concentration of glycerol as used in Loewenstein's medium inhibits the growth of the bovine type, while the human type does not grow well on media in which glycerol is not incorporated. It is evident therefore that in cultural examination several media, with and without glycerol, should be employed in order to ensure optimum growth conditions. If the cultural characteristics of an isolated strain do not allow the type diagnosis, inoculation of a rabbit is the method of choice. According to Jensen, cultures planted for type differentiation should be homogenized with sodium hydroxide, and not with acid, the dilution used for inoculation being selected in a way that assures the growth of well separated colonies. (For details of technic see Jensen.<sup>13</sup>)

Reports on the incidence of *bovine infection* of the human being are very incomplete and vary. It is generally agreed, that the human type prevails in tuberculosis of the lung. Lange<sup>1</sup> and Griffith<sup>9</sup> reported a small number of bovine infections of the lung. While Lange points out that especially people



taking care of cattle are exposed to this type of infection and assumes that the infection takes place by inhalation, Griffith considers the bovine infection of the lung as secondary to a primary intestinal tuberculosis. Primary cervical and mesenteric gland tuberculosis has been shown by Griffith to be associated almost exclusively with bovine infection in England and Scotland; the same observations have been made by Jensen in Denmark for children up to the age of 15 years. In persons above 15 years of age the human type of tubercle bacillus infection prevails. The frequency of cervical gland tuberculosis in children is a direct indication of the extension of bovine tubercle bacillus infection in cattle since milk and milk products are the main source of infection for children. Jensen reported also that in Denmark approximately one-half of tuberculous meningitis occurs in children of 5 years of age or less and that, among those the bovine type of tubercle bacilli is found in 50 per cent. of the patients.

The pathogenicity of the *avian* type of tubercle bacilli for the human is not yet definitely established and the clinical picture not clearly described. According to Loewenstein, avian tubercle bacillus infection exhibits sepsis-like symptoms. This may be the reason that other investigators have failed to recover the avian type of tubercle bacillus in extended series of examinations. This type of tubercle bacillus may be differentiated by its slimy growth in cultures, its pathogenicity for chickens (mammalian tubercle bacilli are not pathogenic for chickens) and its virulence for mice, in which mammalian tubercle bacilli produce a chronic process.

#### SEROLOGICAL DIAGNOSIS OF TUBERCULOSIS.

Specific serum diagnosis depends upon the demonstration of certain changes in the patient's serum involving the presence or absence of substances called antibodies. This term implies in no way that the hypothetical antibodies are connected with the immunological status of the patient; for they are not immune bodies in the sense of diphtheria antitoxin. They are not bactericidal nor do they neutralize tuberculin in the infected animal. All attempts to correlate their presence with the activity of the tuberculous infection, the tuberculin sensitiveness of the patient or the prognosis have failed completely. While the development of antibodies is not so pronounced in tuberculosis as in diseases caused by other bacteria they are suitable substances for the serological diagnosis of tuberculosis. Because the technic is delicate and requires serological experience and because of the uncertainty of the clinical significance serological diagnosis of tuberculosis has not come into general use.

The number of antigens tested at one time or the other is almost unlimited. In the place of living or dead tubercle bacilli antigens prepared and extracted from the organisms have been employed. According to the method used for extraction some antigens have been termed lipoid or protein free extracts. However, none of the methods employed insure that they are really free from such substances but rather poor in content. Most of them must be considered lipo-proteins. Zinsser and Mueller, Laidlow and Dudley and Heidel-

berger<sup>35, 23, 17, 10</sup> have extracted carbohydrates. However, no reports on the clinical application of such antigens have been published.

*Agglutination tests* with the tubercle bacillus are difficult on account of the frequent spontaneous agglutination of acid fast organisms and the difficulty of preparing homogeneous suspensions. Mudd's<sup>22</sup> resuspension method after centrifuging facilitates agglutination tests considerably, but to our knowledge has not been applied for clinical purposes. Precipitin tests have not been tested in series large enough to judge their value and limitations. The complement fixation test is the most practical one devised so far and has been applied more extensively than any other test. The essential principle involved in the complement fixation test for tuberculosis is similar to that in the Wassermann reaction. The results obtained do not depend so much upon the proper selection of the antigens as upon a careful technic. It has been demonstrated that tuberculous sera vary considerably in their complement content, therefore incorrect complement titration leads to errors. The question whether an excess of hemolysin or a sharply titrated hemolytic system should be used is a question of preference for more nonspecific reactions, or less sensitive reactions for weakly positive sera. The more sensitive the antigen the less specific it is. Artificially produced anti-sera cannot be used for titration because they may react entirely different than patient's sera. Antibodies can be produced relatively easily with a number of antigens but there may be no relation between the artificial antitoxins of the animal and those present in human sera. Also human sera contain qualitatively different tuberculous antibodies. Much's theory of partial antigens of a qualitatively different nature, has been confirmed by Dienes, Schoenheit and Pinner.<sup>6</sup>

The interpretation of results in serological tests is made difficult on account of the difference in the classification used by clinicians. Of value are only those reports which include control sera with a large series of tuberculous patients. Reports should also include other laboratory tests such as a positive or negative sputum. With a few exceptions all authors agree that positive serological reactions without clinical symptoms do not permit the diagnosis of tuberculosis.

*Nonspecific Tests.*—A number of *diagnostic tests*, depending upon the demonstration of nonspecific changes in the serum of tuberculous patients have been devised, but none has reached a state of usefulness in practice.

Among the serological tests designated to determine the "activity" of a tuberculous process, the *blood sedimentation test*, developed by Fahraeus<sup>3</sup> and first applied to the examination of tuberculous patients by Westergren<sup>32</sup> has found wide acceptance. Because the result of the test is determined by the status (equilibrium between microorganism and host) of the patient at the time the blood sample is secured and not by the reaction of the patient to an agent, it is evident that the registration of the *changes* in the sedimentation rate by a series of observations is of more value than a single test. However, it is generally agreed that a normal sedimentation rate renders the presence of an active tuberculous process very improbable.

Sedimentation rate of erythrocytes depends upon the suspension stability of uncoagulated blood which in turn is determined by the electric potential differ-

ence between the negatively charged erythrocytes and the positively charged plasma constituents of the blood. Any change in the number of erythrocytes, their cell volume and the hemoglobin content on the one side, and changes in the composition of the plasma on the other side, will lead to a changed sedimentation rate. An alteration in the ratio of albumin to fibrinogen and globulin in the plasma seems to be the dominating influence, because Sterlinger<sup>28</sup> has shown that fibrinogen content and sedimentation rate run strictly parallel.

In the method devised by Westergren the sedimentation rate is measured after 1 hour in terms of distance (normal values 3 to 7 mm. for the adult male and 7 to 11 mm. for the female). Linzenmeyer's method registers the time consumed for the passage from one mark to another (normal values 600, 200 and 250 minutes, respectively).

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## CHAPTER VII.

# PHYSICAL DIAGNOSIS IN PULMONARY TUBERCULOSIS.

GEORGE G. ORNSTEIN AND DAVID ULMAR.

One of the fascinations in the diagnosis of diseases of the lungs is the test of one's skill in the wit and logic that is required to correlate the findings on physical examination with the underlying pulmonary pathology. Here one cannot directly examine the lesion as is the case in a skin disease, but must project the senses as *forms of intellectual antennæ to better comprehend the invisible*. If one's perceptions are correct and interpretations logical, then the whole jigsaw puzzle will fall into a single intelligible pattern—the condition of the underlying lung. This scheme presupposes a certain skill in the interpretations of physical signs as well as an ability to evaluate the mechanism of their production. In the next few pages we propose to outline our methods in this respect. We believe that if this procedure is adhered to, physical diagnosis will cease to be the humdrum ritual and will assume the position of live interest it so rightly deserves. For purposes of clarity and orderliness, the grouping of physical signs is usually put into four divisions: inspection, palpation, percussion and auscultation.

### INSPECTION.

Inspection of the patient often reveals information of considerable importance. The general symmetry of the thorax should be noted. Gross bony deformities such as kyphosis or scoliosis may at times produce secondary changes which can give rise to abnormal auscultatory findings. Mention is sometimes made of the broad chest as opposed to the long narrow chest, the latter occasionally being referred to as the phthisical habitus. As far as its relation to tuberculous infection is concerned, the shape of the thorax is of no consequence. Tubercle bacilli may play equal havoc in any shape of thorax whether the patient have the typical phthisical chest or not. From the point of view, however, of the mechanics of collapse therapy, the general shape of the bony cage may have a profound bearing on the result that is obtained with any one procedure. Thus, where the ratio of the depth of the thorax to its width is such as to make a thoracoplasty a very inefficient means of collapse, this observation of the general shape of the thorax may be extremely significant and its recording important. Of equal significance is the noting of any local asymmetry. Anything which will tend to change the total volume of the thoracic contents will produce corresponding alterations in the thoracic cage. Thus, gross scarring of the lung with its resultant contracture and lessening of lung volume will cause a lessening of the diameters of that thorax. The chest on that side will appear retracted and asymmetrical. Any condition which will diminish lung volume will produce this picture whether it be the scarred contracted lung or the airless atelectatic lung.

Similarly, increased thoracic volume will produce a bulging of the thorax in all its diameters. The commonest cause of this condition is emphysema of the lungs. This is generally bilateral and when marked, produces the barrel-shaped chest. Occasionally this increased lung volume or emphysema may be unilateral as in the case of a ball-valve foreign body in one main bronchus. Here air can enter the lung but because of the valve effect cannot escape. As a result, the lung becomes distended with air so that an increase in size of that thorax may become visible. By the same token fluid in the pleural space, if present in sufficient quantity, may cause a bulge of the chest wall

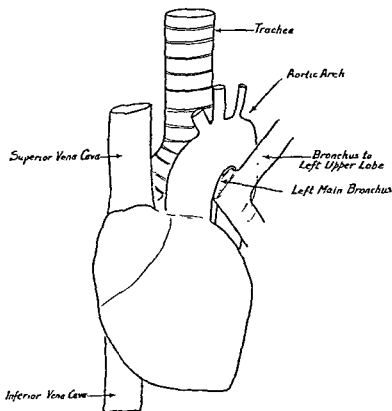


Fig 1

The dynamics of the chest wall may also be interfered with so that on inspection the motion of the chest is found to be impaired. Fluid, possibly because of its sheer weight, is apt to cause restriction of motion. Gross dense scarring, probably because of the guy rope effect of the adhesions, may also impair the mobility of the chest wall.

Occasionally inspection of the patient will reveal localized areas of thoracic edema or venous congestion. Limitations of space and topic prevent a complete discussion of these very interesting conditions. Commonly enough cases can be seen in which there is pressure on the superior vena cava, due either to enlarged lymph nodes or tense abscess pockets. In order to understand them it is essential to keep in mind a clear picture of the anatomy of the region, and especially of the lymphatic and venous drainage systems. A glance at Fig. 1

✓ shows that this pressure can readily occur at the base of the superior vena cava. An enlarging mass in this area is restricted posteriorly by the resistant trachea and on the left by the firm aorta. The soft venous trunk, however, may readily be compressed, giving rise to evidence of obstructed venous flow such as edema of the thoracic wall, head, neck and distended veins. We have recently seen a patient with a cervical rib which caused pressure on the subclavian vein. Edema of the shoulder and arm resulted.

Our discussion to this point has been largely confined to the local condition of the thorax. Of perhaps even greater significance is the information that can be gained from an inspection of the general condition of the patient. The rate and depth of breathing coupled with the degree of cyanosis will give the observer a fairly accurate insight into the amount of pulmonary decompensation. Of course, it is essential to have a knowledge of the fundamental principles of respiratory physiology and interchange of blood gases in order to properly evaluate the observations. Of especial importance is the necessity for a thorough understanding of the profound importance of  $\text{CO}_2$  in the human economy. For a fuller discussion of this the reader is referred to the chapter on Pathological Physiology. We feel that this part of the physical examination is apt to be neglected. A more careful and intelligent check-up on these important points will lead, we believe, to more rational attempts at therapy based on true physiological needs.

### PALPATION.

By means of palpation certain additional information largely of a vibratory nature can be obtained.

**Vocal Fremitus.**—When voice sounds are uttered, the power of their vibration is transmitted to the chest wall and can be felt as vocal fremitus by the palpating hand. This energy has its source in the vibration of the vocal cords of the larynx and is transmitted to the palpating hand by one of two routes, either in a speaking tube fashion down through the bronchial tubes and thence through the lung parenchyma and chest wall, or else directly through the solid structures of the body radiating from the larynx. As is the case in any perception, the stimulus that is received by the palpating hand will be a resultant of the initial energy plus the changes that take place in the transmission from its source to the chest wall. All other things being equal, a loud sound, having greater energy in the input, will be felt as exaggerated tactile fremitus when compared with a weak voice. Where the source of sound is constant, then the character of the fremitus can be affected by the quality of the transmitting medium. In the first place it is essential to remember that the normal lung is a selective transmitter, passing most efficiently the low frequency band around 250 vibrations per second, and damping the higher frequencies. This characteristic will be discussed more fully later. It will therefore be seen that the low bass voice will be felt much more intense than the high pitched soprano voice for the reason that the majority of vibrations of the soprano voice have been damped and do not reach the surface. Conversely, any pathology in the lung parenchyma which will impair its efficiency as a selective transmitter will allow

more of the higher frequencies to pass. *Fremitus* will therefore be increased over that area of pathology. Partial fibrous replacement or consolidation of the parenchyma are examples of this condition. The transmission of this vocal energy can also be influenced by other factors. Thus, a thick heavy chest wall, whether the thickness be due to fat, muscle, or thick pleura, will tend to diminish the amount of vibratory energy which will be felt at the surface. Likewise, transmission through different media is apt to cause a reflection of energy at each surface and thereby block the passage. Thus, fluid in the pleural space gives two reflecting surfaces, one on each side of the fluid pocket, so that *frenitus* is usually effectively stopped in spite of the fact that fluid *per se* is an excellent sound conductor. A pneumothorax space, because of the inability of the energy to be propagated through the air space and thence to the chest wall, also tends to diminish *fremitus*. Plugging of the bronchus, by stopping the speaking tube mode of transmission, allows only the solid structures to act as carriers of the energy. This is a very cumbersome and inefficient method and therefore *fremitus* is markedly diminished or even absent. The surprising thing really is that *fremitus* is felt at all when one considers the small amount of input energy and the massive structures which must be made to vibrate before any stimulus can be perceived.

*Interpretation*—The interpretation of the sensation of *fremitus*, which is elicited by the simple expedient of applying the hand to the thorax while the patient phonates some resonating sound such as 99, will be dependent upon a clear understanding of the factors enumerated above. Thus, the diminished *fremitus* over a woman's thorax is due to the weak input plus the damping of the high frequency vibrations while a man's voice, being stronger and lower-pitched, comes through much more clearly. Normally, *fremitus* is slightly increased over the right upper chest as compared with the left. The simple consideration mentioned above will easily explain this fact. The direct transmission of the vibration from the larynx without intervening structures that are present on the left side will account for the difference.

Suspected increase, diminution, or absence must always raise first the question of the physics of production and transmission so that the alteration in the physical sign may be adequately explained. Only then can the pathology which produced this alteration be intelligently considered.

The palpating hand is also able to detect other changes besides the dynamic *fremitus*. The course of the trachea as it enters the thorax can be readily felt. Its normal position is in the mid line or very slightly to the right. Anything which will cause a shift of the upper mediastinum will alter the course of the tube. This shift may be due to either a push or a pull on the mediastinal partition. Thus, contracture of the scar that is seen in the end stage of a caseous-pneumonic tuberculosis will produce this pull with resultant shift of the mediastinum and malposition of the trachea. Shrinkage of the lung due to absorption of air as in massive atelectasis will cause the same result. A high tension pneumothorax, on the other hand, due to the unequal pleural pressures, will push the mediastinum over toward the opposite side. Fluid may act in a similar fashion. All of these conditions, if they produce a shift of the upper

mediastinum, will cause a palpable deviation of the trachea to the right or left as the case may be. Lymph nodes are also to be felt for. Not only are the cervical and axillary nodes of importance, but also any other nodes which may drain the thoracic space.

Frequently when there has been some long-standing infection or tumor growth within the thorax so that the parietal pleura is involved, nodes may be palpated in the intercostal space adjacent to the area of infection. We have found this node of singular importance in some cases of intrathoracic tumors where biopsy of the palpable node has shown the presence of cancer cells before there was any evidence of metastasis in the axillary group.

### PERCUSSION.

Percussion is the third link in the chain of evidence afforded by physical diagnosis. The eliciting of this sign requires a definite act on the part of the investigator and therefore a certain technic. To make comparisons and in order to properly evaluate the result obtained, it is essential to develop a standard and definite technic. The usual method is to percuss the thorax through the medium of a finger (pleximeter) which is kept in close apposition to the chest wall. Unless this finger is firmly applied and in a similar fashion at all times, variations in note may be obtained which can be very misleading. Careful attention must be paid to this simple but significant detail. This note that is obtained when the chest is percussed may vary in pitch from one that is low and booming to a sound that is relatively high and of short duration. According to these variations in pitch the note is described as resonant, dull or flat, the resonant note being on the low end of the scale and the flat note on the high end. The type of note that is obtained on percussion will be determined by the condition of the underlying tissue. A solid airless tissue acts much in the same fashion as a stiff metal rod that is fixed at one end and plucked at the other end. The vibrations will be very rapid and soon disappear. Similarly, the solid airless tissue responds with a high frequency note of relatively short duration. Air-containing tissue, on the other hand, probably because of its increased softness and flexibility, acts much like the soft and flexible willow reed. Its vibrations are slower; the pitch is lower, and the duration is longer. It can therefore be seen that the percussion note that is obtained will depend upon the ratio between air and solid structures. The normal individual, with air containing lung parenchyma and a normal chest wall, yields a note that is moderately low-pitched and is termed normal resonance. As the proportion of solid tissue increases, regardless of its position, so will the pitch of the percussion note be elevated. The only qualification is that this altered air-solid ratio be within the range of energy that is supplied by the percussion stroke. Thus, a thick muscular chest wall with normal underlying lung will yield a note that is slightly dull as compared with the sound obtained over a thin chest wall. Any pathological condition which produces an analogous thickening will cause similar alterations in the percussion note. Simple thickening of the pleura may produce greater or less degrees of dullness. Fluid between the layers of the pleura usu-



ally alters the percussion note. When present in moderate amounts it may produce flatness. In other words, the structures within range of the percussion blow are completely airless and therefore the note is very high-pitched, or flat. In a similar fashion alteration in the normal air-solid ratio in the lung parenchyma will result in alteration of resonance. Slight fibrous infiltration will give only slight dullness. Marked fibrous replacement will raise the pitch to a greater degree. Complete replacement of the air in the lung through any cause will give a very high pitched note, or flatness. Thus, the airless atelectatic lung or the completely consolidated lung yields flatness on percussion.

*Ratio of Air and Solid.*—The only consideration throughout the whole realm of percussion is the ratio between air and solid and its availability to the percussion stroke. Deep-seated pathology, because of the overlying normal structures, may not be sufficiently energized by the pleximeter to send back its vibration and will therefore be missed. As the surface of the chest wall is approached, the opportunities for detectable changes increase so that the final sound produced is in reality a summation of the various component vibrations. Thus, fluid in the interlobar space, if it can be reached by percussion, may yield a mere dull note while a similar amount of fluid in the outer pleural space adjacent to the chest wall almost invariably will cause flatness. The dull note over the interlobar fluid probably also has an additional explanation. The overlying lung, which has been partially compressed by the fluid sac, contains less air than normal lung and will therefore yield a less resonant note. In other words, the less the air, the higher the pitch and therefore the flatter the note.

*Resonance.*—Increase in resonance can be similarly explained. Any condition which will increase the relative amount of air of the air-solid ratio will increase the resonance. Thus, distended emphysematous lungs usually give a hyperresonant note. Likewise, air in the pleural space will produce a similar hyperresonance. Occasionally this pneumothorax air is contained under more or less increased pressure. When such an area is percussed, the effect is much the same as that produced by bouncing a large tense pneumatic rubber ball on the concrete pavement. The blow causes a sufficient disturbance of the contained air to add to the usual percussion note the overtones which are present in the tense air-pocket. As a result there is a peculiar musical quality to the ensuing resonant note. This is usually described as a tympanitic percussion sound. Whenever obtained it merely means an underlying collection of air under tension so that these additional overtones may be elicited. It has been mentioned by some that this tympanitic note can be obtained over a cavity in the lung. In our experience this has not been the case. When one considers the pathology, it is difficult to understand how a tympanitic note could ever be obtained. The usual cavity that is seen in the end stage of a caseous-pneumonic form of tuberculosis is surrounded by dense scar and fibrous tissue. The pleura, too, is usually markedly thickened. As a result, one percusses relatively airless tissue and not the cavity. The note therefore is usually quite dull. The other type of cavity, which is relatively large, thin-walled and surrounded by normal lung, gives no evidence of its presence on percussion.

acceleration in the velocity of the air jet in the reed pipe there results merely an increase in intensity of the sound. The pitch remains unaltered. With the labial pipe, on the other hand, there will come a time when any further increase in velocity will cause the pitch to jump up an octave. This can readily be demonstrated by blowing across the neck of a ketchup bottle. It can sometimes be demonstrated over the trachea on forced expiration, all of which points against the laryngeal origin of breath sounds. On expiration a similar labial

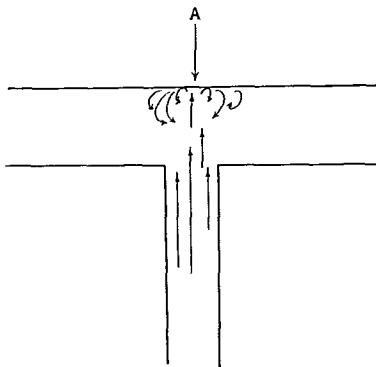


Fig. 4

pipe effect is produced. If one blows through the stem of a T tube as illustrated in Fig. 4, a turbulence is established at *A* which corresponds to the lip of the organ pipe (Fig. 2, *A*). A sound will result. On expiration a similar sound producing mechanism is evoked.

Air rushing out of the bronchi produces the same T tube effect by striking the bronchial wall at Fig. 5, *A*, thus producing a turbulence similar to that produced at Fig. 4, *A*. In addition to the sound produced throughout the bronchial tree at each bifurcation, there is probably also a production of sound in the alveoli themselves. This is somewhat difficult to prove. However, in an experiment recently performed with the coöperation of Frederichs, Wegel and Blattner of the Bell Telephone Laboratory, it would seem that this is actually so. The experiment consisted in passing a constant stream of air from a large chamber through a small tube to another large chamber. The small tube corresponded to the bronchioles, the large chamber to the alveolar sac. A schematic drawing is given to show the arrangement (Fig. 6). The direction of the air flow is shown by arrows. When the sound produced in these

chambers was detected by suitable microphones, a sound similar to vesicular breathing was recorded. Reference will be made later to this experiment.

From the above discussion it can be seen that we believe there is a production of sound throughout the entire bronchial tree down to the terminal lung acinus. Before this sound may be perceived by the listener's ear, however, it must be transmitted through varying thicknesses of lung tissue and chest wall till it reaches the surface of the thorax. The modifications imposed by this transmission exert a profound influence upon the final sound that is heard. Upon these modifications must be based our interpretation of breath sounds. A thorough understanding of the transmission of sound through the chest therefore becomes essential.

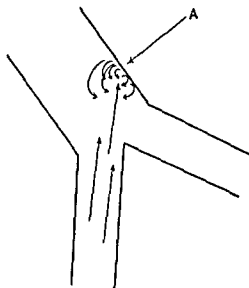


Fig. 5

One of the acoustic characteristics of normal lung parenchyma is the fact that it acts as a selective transmitter, *i. e.*, it transmits efficiently a relatively narrow band of frequencies and tends to suppress or damp all other vibrations. The optimum frequency for transmission through normal lung parenchyma is around 250 to 400 cycles per second, a comparatively low pitched note. It so happens that the sound produced in the bronchial tree is predominantly of a much higher pitch. It ranges between 1,000 to 2,000 cycles per second, although there are frequencies as low as 100 per second. When this high frequency sound radiates through the bronchial wall and reaches the lung parenchyma, the selective transmitter action of this tissue fairly effectively suppresses these higher notes. Consequently only the low frequency bands are passed. This, coupled with the actual production of sound in the alveoli themselves, results in a relatively low-pitched tone, the vesicular breath sound. Normally, with a normal lung parenchyma this low-pitched sound is heard over the entire thorax with the exception of the right apex. Here the power of the bronchial input is so great, due to the close proximity of the trachea to the apex of the lung,

that some of the higher frequencies force themselves through the selective transmitter. As a result a higher pitched sound called broncho-vesicular breathing is heard. But even here, if one allows a sufficient thickness of normal lung to intervene between the large bronchial tubes and the ear, as may be easily done by listening high up in the axilla, the selective transmission again becomes evident and a low pitched or vesicular type of breath sound is heard.

*Lung Parenchyma*—As may be readily surmised, alterations in the physical state of the lung parenchyma affect its sound transmission characteristics as well as its sound production ability. The result may be a profound alteration in the audible breath sound in the particular area affected by the changes. With the appearance of some process which tends to disturb the normal structure of the lung parenchyma, as for example a marked increase in the interstitial tissue

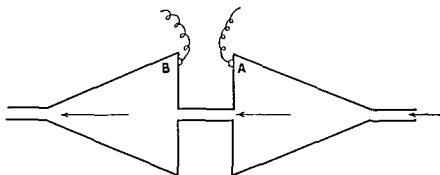


Fig 6

or a productive tuberculous infiltration, there is a corresponding impairment of efficiency of the lung parenchyma as a selective transmitter. With this impairment of function as a selective transmitter, more of the high frequency notes generated in the labial organ-pipe bronchial tube system are permitted to pass through to the chest wall. As a result the pitch of the breath sound is raised and broncho-vesicular breathing is heard. With an increase in this replacement process, to the corresponding detriment of the selective transmitter effect, there is a proportionate increase in the higher frequencies that are heard on the chest wall. When the process has reached its maximum degree and the normal lung parenchyma has been completely solidified, then its function as a sound producer and selective transmitter is completely nullified. Instead of being a selective transmitter it now becomes in reality an excellent transmitter of all sound frequencies. As a result, all of the notes produced in the bronchial tubes are transmitted so that when one auscultates the surface of the chest what one is actually doing is to listen directly to the sound of the air rushing by in the bronchial tubes, listening through the medium of solidified lung which is now functioning as a first-class listening stick. The sound heard is bronchial breathing. The whole affair can be schematically represented by a diagram as in Fig. 7. This conventionalized drawing represents a transverse section of a lung with bronchi cut at various levels and surrounded by lung parenchyma.

At each of the bronchial tubes there is the organ pipe effect with the production of high and low pitch tones, represented on the diagram by *H* and *L* respectively. When the bronchus is surrounded by normal lung parenchyma, the selective transmitter action suppresses the high frequencies. Only the low notes are therefore heard and vesicular breathing is the result as at *A*. This same effect may be noted when there is some pathology centrally located with surrounding normal lung. When some partial replacement of the normal lung parenchyma takes place so that its efficiency both as a selective transmitter and as a sound producer is impaired, then more of the higher frequencies are permitted to pass

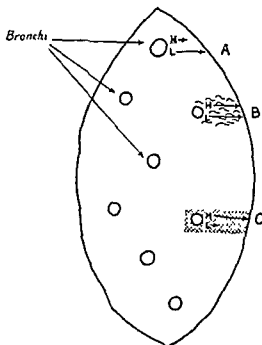


Fig. 7

and broncho-vesicular breathing is heard, as at *B*. When the lung parenchyma is completely solid, as at *C*, then its function as a selective transmitter or sound producer is completely lost. The high notes come through unimpaired and bronchial breathing is heard. It is immaterial as to the cause of this solidification. The consolidated lung of the pneumococcus lobar pneumonia is the classic example. The same end result from the standpoint of physics can be and is seen in the compressed lung of the thoracoplasty case. Here, when the collapse is good, loud breathing of the bronchial type can be heard over the compressed side in spite of the fact that there is relatively little mobility of that lung. The only tenable explanation is that one is listening to the air rushing through the large tubes to the aerated lung, listening through the medium of the compressed and acoustically abnormal functioning lung. The peculiar tubular sound that has been noted in some neoplastic conditions of the lung probably has its explanation in the same mechanism. Here the solid cancerous lung transmits directly the bronchial sound.

*Pathology.*—From the foregoing discussion it can be seen that pathology in the lung parenchyma is bound to result in an alteration of the quality of the audible breath sound, provided, of course, that there is no normal lung intervening between the pathological part and the chest wall that is being auscultated. The corollary that alteration in the quality of the breath sound means pathology in the lung parenchyma is also true with but one very special exception. If there is a large air space such as a cavity in the lung parenchyma or a pneumothorax space outside the lung parenchyma, any energy imparted to this resonating chamber will produce a turbulence of contained air. This turbulence may be

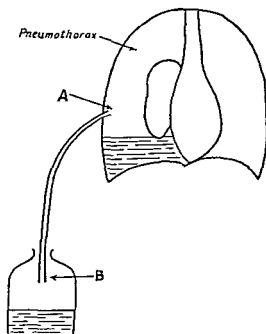


Fig. 8

produced in several ways. If the cavity or pneumothorax space has a bronchus communicating directly with it, then the flow of air in and out will be sufficient to produce this result. Breath sounds of this type are known as amphoric.

Recently we had the privilege of verifying this in a very striking fashion. A patient had a spontaneous pneumothorax in whom the intrapleural pressure was such as to require a release of the tension. This was done by means of a tube leading from the thorax (Fig. 8, *A*) to a bottle where the end of the tube was closed by a water seal (Fig. 8, *B*). When the bottle was lowered so that the end of the tube, *B*, was above the fluid level, then the sound heard over the bottle was identical with the sound heard over the pneumothorax.

If there is no patent bronchus leading to the resonator, the overtones may not be produced. In the lung parenchyma with a check-valve cavity these sounds are never heard. In the pneumothorax space, however, the overtones may be heard if the proper conditions are present. These conditions predicate a strand-like adhesion between the visceral and parietal layers of the pleura and a suffi-

cient intra-thoracic pressure to keep the adhesion taut. The act of respiration now has the effect of causing some vibration of the band-like adhesion. The result is similar to bowing a violin string. The energy transmitted to the resonating chamber is sufficient to produce the characteristic alteration of the breath sound. This effect is frequently observed in the course of pneumothorax treatments especially after refill.

Where there is a propagation of sound from any distant source, many different things may happen to that sound before it reaches the listener's ear. In the preceding paragraphs have been discussed the effects of variation in the selective transmitter effect of the lung parenchyma. There remain to be considered the various other conditions which may affect the audible breath sounds. Following the sound from its source of production to its ultimate destination on the chest wall, one finds that the main effect of these other conditions is a variation in the intensity or duration of the sound rather than an alteration in the quality. Abnormal conditions may occur at the very source of production of the sound itself. Thus, if more air than normal enters the bronchi, the organ pipes will be blown more loudly (*exaggerated breathing, vicarious emphysema*). If all other conditions are equal, then the resultant breath sound will be more intense than usual. This condition can be readily observed where one lung is compensating for the incapacity of the other lung, as in a pneumothorax for example. Localized conditions of this sort may also be observed where some deep pathology is causing an overwork of the more superficial lung tissue. At times this may be the only evidence on physical examination of any pulmonary pathology. Where the chest wall is very thin and little energy is absorbed in the radiation of the sound, a loud breath murmur is the result even though the energy at the source was no greater than normal.

Just as there can be an increase in the intensity of the breath sound, so also may there be a decrease in the intensity. If the sound producing mechanism is not properly actuated, there is apt to result a diminution of the loudness of the resulting sound. Any obstruction to the normal free flow of air in the bronchial tubes will cause this effect. This obstruction may be due either to a narrowing of the lumen on account of pressure on the bronchus from without or to actual obstruction of the lumen due to a piling up of bronchial secretion or to tumorous growth. Pressure from without may be caused by enlarged nodes. Quite commonly enlargement of the aortic arch will press on the bronchus to the left upper lobe, narrowing it sufficiently to cause diminished breathing over the area of the lung supplied by that bronchus. If the dilation is distal to the aortic valves, this simple lung sign may be the only evidence of the vascular lesion. Obstruction from within the bronchus due to mucus may usually be relieved by coughing. When the diminished breathing persists over the local area supplied by the bronchus, the question of some tumor mass or foreign body obstructing the airway must always be raised. Loss of elasticity as seen in emphysema will impair the normal to and fro flow and churning of air in the lung parenchyma so that sound production is diminished. Lack of aëration due to any other cause will produce similar results. Thus, paralysis of muscle groups with corresponding loss of chest mobility may lead to diminished breathing over that area. A

very common condition of this sort is the diminished breathing at the base of the lung following paralysis of the diaphragm due to phrenic neurectomy. Usually this auscultatory finding gives an excellent insight into the physiological result of a phrenic avulsion.

Certain types of inflammatory reaction by the very nature of their pathology are apt to interfere with sound production and propagation so that the breath sound is made feeble. Exudative reactions in the lung parenchyma, probably because of the intense inflammatory edema of the alveolar walls, produce a felt-pad damper effect which fairly effectively prevents the sound from reaching the surface. This condition is seen early in lobar pneumonia. Later, when the exudate has become stiffened and coagulated there is the perfect sound transmission which results in bronchial breathing. The exudative type of tuberculosis has a similar pathology and a similar diminution of breathing. In the benign exudative form of tuberculosis, however, there is never any coagulation so that seldom is bronchial breathing heard. The breath sound remains diminished.

Once through the lung parenchyma, the breath sound must traverse pleura and chest wall in order to be heard. The thicker the chest wall, the more the energy that will be absorbed and, therefore, the less intense the audible sound. Whether the thick wall be due to muscle or thick pleura is immaterial. The result is the same as far as sound transmission is concerned. Fluid in the pleural space, in spite of its excellent sound transmission qualities as witnessed by submarine signalling devices, effectively prevents the transmission of sound because of the reflection at each surface. Pneumothorax air diminishes the intensity possible for the same reason.

*Recapitulation*—To recapitulate what has been stated in the previous pages, there is a production of sound throughout the bronchial tree system. This sound is composed of high and low frequencies. Normal lung parenchyma, acting as a selective transmitter, is able to suppress the high frequencies so that a low-pitched vesicular breath sound is heard. With pathology in the lung parenchyma so that its efficiency as a selective transmitter is impaired, more of the high frequencies come through till finally with complete consolidation and therefore complete impairment of the selective transmitter effect, all the high notes come through and bronchial breathing is heard. Pathology in the bronchus, having nothing to do with parenchyma, can only affect the intensity of the breath sound and never its quality.

Where the value of the breath sounds is of such great weight in the interpretation of pathology, it is of extreme importance that these variations in breath sounds be recognized correctly. The proper cognizance of the different types of breathing has always seemed to be the bugaboo of medical students and of many practitioners. The reason for this difficulty is probably because of the attempt to differentiate the sounds on the basis of differences in quality. This is a notoriously difficult thing to do and is an utter impossibility when any attempt is made to convey to another person the quality of the sound that has been heard by the listener. It is much the same as trying to describe the quality of a piano note or a violin note. From experience one learns to recognize each sound, but still finds it impossible to convey to a second person the auditory impression of



quality. It is probably for this reason that the statement is often uttered that the correct recognition of breath sounds can only be made after years of experience. We most emphatically do not agree with this opinion and base our assertion upon an extended experience in undergraduate and post-graduate instruction.

Any sound may be analyzed on the basis of four components: quality, intensity, duration and pitch. The various breath sounds are no exception to this mode of investigation.

**Vesicular Breathing.**—Scanning vesicular breathing with this in view, one notes that the quality of the sound on inspiration has been likened by some romantic soul to the rustling of wind through leafy trees and is termed vesicular in quality. On expiration, the quality is slightly different and is termed blowing. The intensity of the sound is a very variable quantity, and is dependent upon factors which have been mentioned previously. As to duration, the inspiratory sound generally lasts through the entire inspiratory cycle. The expiratory murmur, starting at the beginning of the expiratory cycle, is generally much shorter in duration, but may at times last for the entire expiration cycle. The general pitch of vesicular breathing is low, expiration being of a lower pitch than inspiration. If one were to represent the relative degrees of pitch by plus marks, inspiration might be designated by 2+ and expiration by 1+.

**Bronchial Breathing.**—Bronchial breathing may be similarly analyzed. Its quality is tubular or bronchial on both inspiration and expiration. The intensity is variable. The inspiratory sound stops abruptly before the completion of the inspiratory cycle. The expiratory sound starts coincidently with the expiratory cycle and may last the entire length of expiration. The pitch of bronchial breathing is very high, expiration being even higher than inspiration. With the conventional plus signs, inspiration may be designated by 4+ and expiration by 6+.




**Broncho-vesicular Breathing.**—Broncho-vesicular breathing is an average of the two previous types. Its component characteristics will vary depending upon which particular element predominates, the vesicular or the bronchial. With marked bronchial attributes there will be no particular difficulty in differentiation. The errors arise when there are but slight changes from the normal vesicular murmur. With the difficulties that are normally encountered when one endeavors to differentiate sounds on the basis of quality it will be seen how immeasurably complicated now becomes the problem. With a variable bronchial component, quality as a means of differentiation is practically useless. Similar difficulties are noted with regard to duration and intensity of sound. The only component which is of real value and which can be implicitly relied upon is the pitch of the sound. Inasmuch as bronchial breathing is a relatively high-pitched sound, the addition of any bronchial component, no matter how slight, is bound to raise the pitch of the vesicular murmur. The expiratory sound of bronchial breathing is considerably higher in pitch than the inspiratory sound. It can therefore be seen that the expiratory murmur of vesicular breathing will have a greater relative and absolute elevation of pitch when combined with bronchial sound than will the inspiratory murmur. As a result the pitch of expiration is the same or higher than that of inspiration, whereas in vesicular breathing the pitch of expiration is always lower.

Using again the conventional plus marks, inspiration might be designated by 3+ and expiration by 3+ or 4+.

A tabulation of the above remarks is given below:

A glance at Table I immediately shows that intensity and duration of sound are of little value as aids in the differentiation of breath sounds except in bronchial breathing where there is a pause between inspiration and expiration. As to quality, here one runs into considerable difficulty. Just as one flounders about in trying to describe the piano note, so one is unable to describe vesicular or bronchial breathing other than to call them vesicular or bronchial in quality. With pitch of sound, however, the matter is entirely different. Aside from the differences in general tone level among the various breath sounds, there is also

TABLE I

		Quality	Intensity	Duration	Pitch
Vesicular Br.	Inspiration Expiration	Vesicular Blowing	Variable		++ +
Bronchial Br	Inspiration Expiration	Tubular Tubular	Variable		+++++ ++++++
Bron. Ves. Br.	Inspiration Expiration	Mixed Mixed	Variable		+++ +++

to be noted the differences in pitch of expiration and inspiration. It will be seen that when one compares the pitch of expiration with the pitch of inspiration in vesicular breathing, the former is lower in pitch. In the other types of breath sounds that have been described, this pitch relationship does not hold. In bronchial breathing expiration is very much higher in pitch than inspiration. In broncho-vesicular breathing the expiration is at least equal to inspiration in pitch and is usually higher. This simple method of differentiation of breath sounds on the basis of pitch is a very reliable one and is easily mastered in short order by the purest tyro. No musical ability is necessary.

Although one cannot describe the piano note, one can easily state whether the note is high C, middle C or low C. And so with the breath sounds. Although the quality cannot be described, the pitch can be noted. Any breath sound whose pitch of expiration equals or goes higher than the pitch of inspiration can no longer be considered vesicular breathing. Vesicular breathing always has a lower-pitched expiration. The only pitfall to be avoided is intensity. To the inexperienced, an intense sound may sometimes be mistaken for a high-pitched sound. The method of eliciting these sounds is simple. One listens while the patient breathes quietly. The pitch of inspiration and expiration at the single spot where the chest is being auscultated is then compared. If expiration is equal or higher in pitch, then the sound is no longer vesicular.

The explanation of these changes in pitch is not definitely established. If two organ pipes of identical pitch are sounded over a common resonator, as in Fig. 9, the fundamental note will occur in opposite phase in each pipe. As a

result it will be neutralized and only the overtones, of higher pitch, will be heard. Perhaps this will explain the higher pitch of bronchial expiration, the dichotomously divided bronchi corresponding to the two pipes of identical pitch and the single bronchial stem corresponding to the common resonator. The reason for the lower pitch of vesicular expiration is even less well understood. In the experiment alluded to in Fig. 6, the sound picked up at *A* was lower in pitch than the sound produced at *B*. This would coincide exactly with the conditions as found in normal vesicular breathing. While it does not tell the mechanism, it at least seems to indicate that it is due to some set of factors in the alveoli and terminal tubules themselves.

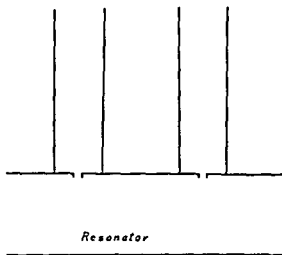


Fig. 9

**Amphoric and Cavernous Breathing.**—Vesicular, broncho-vesicular and bronchial breathing have been discussed. There remains to be considered merely *amphoric and cavernous breathing*. These two types of breath sound, as has been mentioned previously, are caused by the overtones of the vibrating air in resonating cavities. They are of a somewhat musical character, amphoric breathing being of a relatively high pitch and cavernous breathing being low in pitch. Once heard they are not easily forgotten. Amphoric breathing can be perfectly imitated by blowing across the neck of an empty bottle. Cavernous breathing is exceedingly rare. Because of its low pitch it is apt to be confused with exaggerated vesicular breathing but may be readily differentiated by means of voice and whisper sounds which will be discussed below. Frequently amphoric or cavernous overtones are added to bronchial sounds so that the resultant mixture is termed *broncho-amphoric* or *broncho-cavernous breathing*.

**Voice Sounds.**—Whispered voice and spoken voice sounds follow the same principles that have been laid down for breath sounds. When the usual "ninety-nine" is phonated, the fundamental note is of a frequency somewhere in the neighborhood of 250 cycles per second. The overtones extend up to 900-1000 cycles. These overtones are responsible for the clear and characteristic quality of the voice, its *klang* or *timbre*.

**Normal Vocal Resonance.**—When the lung parenchyma is normal and its selective transmitter effect unimpaired, the majority of the overtones are suppressed upon attempting to pass through the selective barrier. As a result one hears only the fundamental note without the overtones that give the clear timbre. The “ninety-nine,” while recognizable, has a very “mushy” quality and lacks the clear crispness of the normal sound. This is called normal vocal resonance.

**Bronchophony.**—With the appearance of pathology in the lung parenchyma and the concomitant loss of efficiency of its selective transmission quality, more of the higher frequency overtones come through. The sound begins to clarify and become more distinct and is termed bronchophony.

**Pectoriloquy.**—With the progression of this affair the final degree is reached in which the lung parenchyma is completely consolidated. Here the selective transmitter effect is entirely lost, all the overtones come through and the sound that is heard is clear, distinct and easily recognizable. This is known as bronchial voice sound or pectoriloquy. When heard it gives the listener the impression of being uttered just beneath the ear instead of in the larynx some distance away. This is so because of the excellent sound conduction from larynx to chest wall *via* speaking tube bronchi and listening stick solidified lung tissue.

Just as the energy of the breath sound is able to produce a turbulence of air in a resonator so that a cavernous or amphoric quality is added to the sound, so also the impression of voice energy on a resonator will add similar overtones to the voice sound that is heard over the chest wall. Depending upon factors mentioned in the discussion of breath sounds, there will be heard either an amphoric voice sound or a cavernous voice sound. As has been previously stated, this cavernous voice or whisper sound forms an easy method of differentiating the cavernous breath sound from exaggerated vesicular breathing. The whisper or spoken voice heard with vesicular breathing has the mushy quality alluded to previously. With cavernous breathing, on the other hand, the whisper or voice sound does not have this indistinct quality inasmuch as it is not filtered by normal lung parenchyma. It is fairly sharp and in addition has the low-pitched overtones of the cavern through which it has passed.

**Adventitious Sounds (Râles).**—In addition to the voice and breath sounds that have been described, there are also occasionally heard certain adventitious sounds or râles. Although sometimes classified according to their sound as dry or moist, all râles are moist in that they are due to fluid or secretion in the lung. The type of râle that is heard will be more or less dependent upon its site of production. The mechanism that is usually involved in the production of this adventitious sound is the bursting of a bubble of fluid with a sudden momentary click as the surface film ruptures. Depending upon the size of the bubble, which, in turn, within limits, will be a factor of the size of the space in which it is formed, will depend the size of the râle that is heard. Secretion in the very fine terminal bronchioles, because of the physical limitation of space, will produce a very small bubble and therefore a very small or fine râle.

Inasmuch as the production of the râle requires a difference in intrabronchial pressure in order to cause a bursting of the bubble, it follows that occasionally

the pressure changes on quiet breathing are not sufficient to produce the desired result. It is sometimes necessary to augment the pressure differences by means of some definite act such as coughing. The tremendous and sudden alteration of intrabronchial air tension during cough generally suffices to click the air through the fluid and thus cause the sound. It is essential to remember this simple fact and to have the patient cough in order to elicit these latent râles.

Very fine râles, being produced in the peripheral endings of the bronchial tree, are usually heard when there is some parenchymal pathology. They are commonly noted in early exudative reactions in the lung parenchyma, as, for example, in the early stage of lobar pneumonia or in the exudative form of tuberculosis. Frequently they may be the only positive auscultatory sign that can be elicited, the power of their input being sufficiently strong to carry them to the surface whereas the breath sounds are suppressed for reasons that have been previously discussed. Incidentally, the reasons given by some authors<sup>3</sup> for the production of this very fine type of râle illustrate how a fallacy may gain entrance into medical literature and be perpetuated. It was at one time considered that this crepitant râle, as it is sometimes called, was caused by the snapping apart after cough of the sticky alveolar walls. A very superficial knowledge of pathology, however, soon demonstrates that this cannot possibly be so. The alveolar walls, instead of being stuck together, are usually widely separated by an intraalveolar exudate so that any possibility of their being stuck together and then separated by cough is utterly out of the question.

As the exudate or fluid appears in larger tubules or lung spaces, the size of the bubble and its resultant râle increases. Accordingly there may be noted medium-sized or large-sized râles, the latter being sometimes termed coarse mucous râles. The coarse bubble which results in the coarse râle requires a fairly large space for its production. It is usually heard where there is some breaking down of lung tissue with the resultant cavitation and liquefaction. As bubbles are formed and burst in still larger antra or cavities, the râles produced thereby may have added to their normal quality the additional overtones of the resonating chamber in which they are produced. This type of râle is known as the tinkling râle. It is commonly heard in spontaneous hydropneumothorax cases or in patients with large antra where there is a bronchus opening beneath a fluid level so that air may be bubbled through the fluid to produce the râle. They may be readily reproduced by bubbling air through fluid in a jug that is half full of the liquid.

In addition to the question of the size of the râle it is of some importance to recognize the pitch of the râle. Bubbles produced in a thick stiff fluid will have a short rapid vibration when they rupture whereas those produced in a thin watery solution will have a longer and slower vibration. The mechanism is similar to the vibrating rods mentioned in the section on percussion and in fact is used in certain laboratories during precise experiments on sound. It so happens that with pathology in the lung parenchyma the secretion of fluid that is present is usually quite thick and viscid. The râle, therefore, is high in pitch. This is of considerable help where the quality of the breath sound cannot be

determined as, for example, in early lobar pneumonia or in the exudative form of tuberculosis. Here the very high pitch of the râle immediately spells pathology in the lung parenchyma. Where the fluid, on the other hand, is not due to intrinsic pulmonary pathology but to some extraneous cause such as heart failure, for example, the viscosity of the fluid is very much less. While mucus is very thick and tenacious, edema fluid is almost watery in consistency. As a result the râle that is heard has a distinctly lower pitch.

**Musical Râles.**—The appearance of secretion in the larger bronchi is usually insufficient to so completely block the tube that the inspired air may bubble through it. Instead, the moisture may gather along the side of the bronchus so that when the tidal air flows in and out it causes a continuous vibration of the secretion similar to a vibrating reed in a horn. As a result an entirely different adventitious sound is produced. Instead of being momentary and clicking it is prolonged and musical and high-pitched. This type of râle is known as the sibilant or sonorous râle, the former being of a relatively higher pitch than the latter. They are heard in these larger bronchi whenever there is excessive secretion irrespective of the cause. Thus, inflammatory changes, as in attacks of bronchitis, or hypersecretion in allergic states such as asthma, will cause this type of adventitious sound. Because of the distribution of the pathology the râles in both these conditions are generalized although in the bronchitides there may be some local area where the râles are more numerous than elsewhere. Definite localized areas of sibilant or sonorous râles may also be heard when the increased secretion is definitely limited to that area. Partial obstruction of a bronchus so that there is imperfect drainage is a common cause of this finding. It is probably because of this fact, too, that gross bony deformities of the thorax may sometimes produce local changes with râles.

**Friction Sounds.**—In addition to the adventitious sounds mentioned above there are occasionally heard other sounds which must be noted. At times a coarse grating to and fro friction sound is heard synchronous with respiratory movement. This is due to the rubbing of the inflamed pleural surfaces and corresponds to a similar tactile sensation.

**Muscle Sounds.**—At times a very confusing element is added to the auscultatory findings by certain sounds that have their origin in the contraction of the muscle bundles of the chest wall. These muscle sounds simulate fine râles. They can be differentiated from true râles by having the patient refrain from breathing and then moving the muscles involved. If the adventitious sounds are still heard, they are, perforce, due to some muscle origin inasmuch as the lung is not functioning at that particular moment as a sound-producing organ.

### STETHOSCOPE.

Before closing the section on auscultation it might be advisable to say a few words regarding the stethoscope that is used. Unfortunately, stethoscopes have been designed by pipe benders and instrument makers rather than by sound transmission engineers. As a result devices of various acoustic characteristics are in common use, some bad and others not quite so bad. Through repeated use

the operator in most instances has learned to interpret the sound and compensate for the deficiencies of his instrument. Inasmuch as the breath sounds are all within the 2000 cycle range it is unnecessary to have a device which will be efficient at higher frequencies. The majority of instruments, with their long rubber tubing, and some with peculiar diaphragms and resonating chambers, are apt to have an abnormally low natural frequency. As a result, the low notes corresponding to this natural frequency are transmitted very well while the higher frequencies that may be present in the breath sound are not so efficiently conveyed to the listener. Inasmuch as it is the change from the normal that is of importance and since these changes from the normal predicate higher frequency sounds, it follows that the stethoscope with the low natural frequency will not be as efficient as the stethoscope whose natural frequency approaches that of the higher pitched pathological breath sounds. A very common cause of this low frequency is long rubber tubing. It is acoustically inadvisable to have this tubing longer than 12 to 15 inches. In experiments at the Bell Laboratory we found that the rubber tubing functioned as a resonator, the longer the tubing the lower its natural period of frequency. Excessive length of tubing probably also causes some dissipation of energy so that the sound becomes more feeble. Where one is dealing with a sound which is near the lower limit of audibility, these factors are of considerable importance. Along this same line might be mentioned the necessity for a quiet environment in order to auscultate the chest. In the competition for the listener's perception the breath sound is easily worsted by any extraneous noise which happens to be louder. If possible to obtain, a soundproof examining room is the ideal solution.

On the previous pages have been outlined our methods of reasoning in the interpretation of physical signs in the chest. It will be noted that reference to specific cases or conditions has been avoided except as pertaining to the illustration of some particular point under discussion. Emphasis has been laid rather on the reasons for the various physical signs and the actual physics of their production. It is firmly believed that the approach to the solution of problems encountered in chest diagnosis should be made in the same fashion. Dullness, broncho-vesicular breathing and râles over an upper lobe should not spell tuberculosis for the investigator. Rather, should they raise the question as to reasons why those particular signs are present. How is the percussion note changed, what is the physics of production of the broncho-vesicular breathing, why the râles? From this point it is but a simple step to piece out the various parts of the puzzle to portray some pathological condition which will adequately explain the physical signs. Once the pathology has been established the judgment and clinical experience of the observer are utilized to present the most likely cause of that pathology. Thus may a diagnosis be established. Short cuts or omissions from this logical plan lead only to haphazard "hunch" diagnosis and eventual error. Adherence to this scheme of reasoning is sure to lead to logical and clear thinking. A lively interest will thereby be engendered in this phase of diagnosis of disease. This is bound not only to improve the skill of the observer but also to advance the art and science of physical diagnosis.

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Quoting Laennec



## CHAPTER VIII.

### PHYSICAL DIAGNOSIS OF PULMONARY TUBERCULOSIS—Continued.

GEORGE G. ORNSTEIN AND DAVID ULMAR

**Diagnosis.**—The diagnosis of tuberculosis is made by no trick of legerdemain nor by any royal short cut. The final conclusion must be based on the proper evaluation and interpretation of the various bits of information gleaned by the investigator from the examination of the patient. In this process of reasoning, all possible aids must be considered and used. With the improvement in technical adjuncts and a broadening of vision in their use, the clinician now has at his disposal a far greater advantage than did his predecessor of but a few years ago. With this advantage has come a feeling of security to some and a tendency to lower the acuity with which the various bits of information are sought for. Now as then, all details are of value. The history of the patient, the physical examination of the patient, the x-ray of the patient and the laboratory findings are all apt to yield details which cannot be overlooked. In that order will they be discussed in the pages to follow.

#### HISTORY TAKING IN TUBERCULOSIS.

**History.**—The most valuable leads in the diagnosis of pulmonary tuberculosis may be obtained through the writings of a good history. There is no method of examination that will make the practitioner more suspicious than his familiarization with the ordinary symptoms associated with the disease. We wish to stress here that through their recognition a diagnosis of tuberculosis may be made more frequently than through the aid of the physical examination.

#### SYMPTOMS OF TOXEMIA.

The symptoms of the disease vary considerably, dependent upon whether the onset is acute or insidious. With the acute onset there is a very toxic picture simulating the acute respiratory infections. In the insidious onset the symptoms are hardly recognizable and are frequently overlooked by both the patient and the doctor.

The symptoms due to toxemia are many but not all are constantly present. The frequent ones are general malaise, lack of strength, fatigue, increases in temperature and pulse rate, night sweats, digestive disturbances and loss of weight. These symptoms may occur with any focal area of infection as, for example, infection of the tonsil. They merely indicate irritation of the central autonomic nervous system due to some cause somewhere in the body. Only when the symptoms cannot be accounted for by some definite area of focal infection should tuberculosis be thought of.

In the past, the above symptoms have been used as the criteria for the determination of clinical activity in pulmonary tuberculosis. Such interpretation is correct. Unfortunately the prognosis in tuberculous pulmonary disease has also been based upon the presence of the symptoms of toxemia. There is no objection to such a procedure where these symptoms are present. The danger is in their absence. "No symptoms" should not warrant a good prognosis. In the chronic phase of caseous-pneumonic tuberculosis the caseous material has been expectorated with resulting cavity formation in the lung. In this phase there may be few or no symptoms and patients frequently not only add a good deal of weight but also regain considerable strength. However, the prognosis is poor in spite of the absence of symptoms. Unless the cavities are closed the patients are doomed to die. A fuller discussion of these important points will be given later. Therefore one must look upon positive symptoms of toxemia merely as the indicators of activity of the disease and depend upon the character of the tuberculous pathology as the arbiter of prognosis.

### REFLEX SYMPTOMS.

There is a group of symptoms reflex in origin which is very suggestive of pulmonary irritation. These symptoms are often present in pulmonary tuberculosis, especially in the insidious forms of phthisis. They are valuable aids in diagnosis. We are indebted to Pottenger<sup>1</sup> for a probable explanation of these symptoms. Pottenger states "We must conceive in studying the symptomatology of tuberculosis of there being constant forces at work to disturb the balance between para-sympathetics and sympathetics which result now in increased parasympathetics, and, again, in increased sympathetic tones. In this way we can understand the variability of the symptoms which are present not only in tuberculosis but in all inflammatory diseases of internal viscera. The same nerve influences can be worked out for each disease."

We agree with Pottenger on the frequency of these symptoms of reflex origin. Their recognition is frequently the first lead in the diagnosis of tuberculosis. These symptoms are not constant and their duration varies in different individuals. Our impression is that the symptoms appear with fresh extension of the disease.

Reflex symptoms are most noticeable in productive tuberculosis where cough and expectoration are either absent or not bothersome. The patients therefore seek relief for these reflex symptoms and are not suspicious of the pulmonary disease. This accounts for the large number of cases that are referred to the tuberculosis clinic from any active gastro-enterological service.

**Gastric Disturbances.**—Gastric disturbances are often complained of. The stomach is irritable and with the entrance of food a spasm occurs at both the pylorus and the fundus. After a few mouthfuls there is a feeling of being "filled up to the neck." We speak of it as a "quick filling of the stomach." The stomach when visualized by a barium meal is small and round. There is little escape of stomach contents. Finally there is some relaxation with belching and occasionally regurgitation. There is an associated hyperchlorhydria. These phenomena may

be due to an overstimulation of the vagus. With such manifestations one can understand why patients seek relief at the hands of the gastro-enterologists who usually find the pulmonary disease during fluoroscopic examination.

**Hoarseness.**—Hoarseness, fogging and tickling in the larynx are also a frequent complaint. They may be reflex in origin and are apt to lead the patient to the laryngologist. The hoarseness rapidly subsides only to reappear again after a short period of time. Complete aphonia may occur. However, hoarseness is more common. Pottenger<sup>2</sup> claims that the afferent impulses travel centralwards through the pulmonary branches of the vagus. The efferent impulses pass through either the superior or recurrent laryngeal nerves. When the superior laryngeal nerve is involved there is a relaxed condition of the cords, whereas recurrent laryngeal nerve irritation produces an interference in adduction. We have seen these phenomena and have discussed them with the laryngologists who are always skeptical. A singer was told there was interference in the adduction of her cords because of temperament. At various times a hoarseness would occur which interfered considerably with her career. She became suspicious of her lungs and, on examination, was found to have tuberculosis.

Tickling in the larynx occurs commonly and causes a dry, hacking cough. The path of this reflex is through the laryngeal branches of the vagus nerve. Again the patient may become misdirected and have attention centered on the pharynx and larynx. Pottenger<sup>3</sup> has stressed this early symptom. Before any surgical procedure for the relief of this symptom is attempted, pulmonary tuberculosis should be ruled out.

**Shoulder and Chest Pains.**—Shoulder and chest pains are also commonly complained of. The pain is most often in the shoulder blade though it may occur in any part of the thorax. There is no constant area and its duration varies. The pain is rarely persistent. Pottenger<sup>4</sup> states: "The reflex sensory disturbance expresses itself in the muscles and superficial tissues supplied by the cervical nerves and the third to the fifth thoracic zones shown by Head. This gives discomfort over the apices of the lungs over the third to fifth interspaces anteriorly and in the scapular region posteriorly."

**Flushing of the face** is reflex in origin and produced by a dilation of the blood-vessels of the face, head and ear. Pottenger<sup>5</sup> states, "The irritation causing it in the face passes through the vagus to mediate with the fifth cranial and in the ear through the sympathetics and the third cervical spinal nerve."

The above reflex symptoms should always suggest the probability of pulmonary disease.

There are a few symptoms caused by the *tuberculous process* in the lung. These symptoms are most important. Some of them, like *hemoptysis* and *pleural effusion*, are almost pathognomonic of the disease.

**Hemoptysis and Blood-streaked Sputum.**—The expectoration of blood is a most valuable symptom in the diagnosis of tuberculosis. Fortunately, hemoptysis occurs in all stages and types of pulmonary tuberculosis. In minimal lesions it may be the only symptom noticed. We should not differentiate between blood-streaked sputum and hemoptysis. The occurrence of either is almost pathog-

nomonic of pulmonary tuberculosis. Because of the preponderance of tuberculosis in chronic pulmonary diseases bloody expectoration should always first suggest tuberculosis. Other pulmonary conditions are often associated with hemoptysis. However, all the various abnormalities combined are small in number compared with the prevalence of tuberculosis. Hemoptysis in fact is more common in some of the diseases as, for example, bronchiectasis, lung abscess or pulmonary neoplasm. The occurrence of the latter three conditions though not uncommon is rather rare in relationship with the frequency of tuberculosis. Other pulmonary affairs which can also cause hemoptysis are aneurism, cardiac disease, tracheo-bronchial syphilis, infarction and the various mycotic infections of the lungs.

A good clinical rule to follow is to associate hemoptysis with pulmonary tuberculosis until another diagnosis can be established.

**Pleural Effusion.**—The sudden appearance of a *pleural effusion* is very suggestive of tuberculosis. The involvement of the pleura is usually secondary to pulmonary tuberculosis. The signs of pulmonary disease are masked by the effusion. Pleural effusion is found to occur with exudative forms of tuberculosis in which rapid resolution frequently takes place.

With the absorption of the pleural exudate there is a parallel resolving process going on in the lung which may leave no trace of the disease. When resolution of the pulmonary process is slow, the disease in the lung may be visualized following the absorption of the pleural exudate. Pleural effusions do not often occur in the chronic types of tuberculosis. Although pleural effusions are secondary to pulmonary involvement, it is not necessary that the lung affair be extensive. A minute sub-pleural tubercle may rupture into the pleural space and thus release sufficient antigen to cause the allergic transudation of fluid. This type of effusion generally clears up rapidly. With a long drawn-out affair in the pleura there is more apt to be extensive underlying pulmonary pathology which is the cause of the persistence of the pleural pathology.

**Pleural Pain.**—In addition to the vague inconstant chest or shoulder pain due to reflex causes, there is a very definite chest pain due to involvement of the pleura itself. Fortunately for the comfort of the patient involvement of the lung parenchyma itself produces no symptoms. It is only when the process reaches the pleural membrane that pain may become evident. The pain that is noted is apt to be severe in character. It is characterized by its relation to respiratory movements, increased motion causing increased pain. Pleural involvement for any cause is apt to produce pleural pain.

**Expectoration.**—Productive expectoration is not always present in tuberculosis. Its absence or presence depends on the character of the tuberculous pathology. Sputum is plentiful in the caseous-pneumonic and scant in both the productive and clearing exudative forms. In exudative tuberculosis, where there is comparatively little lung necrosis, tubercle bacilli are found only in the first days of the infection and search for them must be made during the period when phlegm is obtainable. Because cough and expectoration may stop abruptly, we advise searching for bacilli as soon as exudative tuberculosis is suspected. Some patients do not expectorate but unconsciously swallow their phlegm. When questioned

they insist they do not expectorate. Pressed by the attendants for specimens of sputum, saliva or naso-pharyngeal secretions are submitted for examination. It need hardly be mentioned that they are reported bacilli-free.



Fig. 10.—A young adult with both physical signs and x-ray of an extensive tuberculosis of the left lung, coughs but does not expectorate. Whatever material he submits for demonstration of tubercle bacilli is reported negative. In thirteen examinations, eight of which were concentrated specimens, no tubercle bacilli are demonstrable. Gastric lavage was performed and many tubercle bacilli were seen in the gastric contents.

It has been the practice in both the Metropolitan (N. Y.) and the Sea View Hospitals to examine the gastric contents for tubercle bacilli in all reported sputum negative cases.

Ulmur and Ornstein<sup>6</sup> in a series of 287 cases in whom there were repeated negative sputum examinations, approximately 20 per cent. yielded tubercle bacilli on examination of the gastric contents.

The following cases demonstrate the value of gastric lavage for the demonstration of tubercle bacilli:

CASE I.—A young male, white, who had been ill the past three years, was admitted to the hospital complaining of cough, fatigue, weakness and loss of

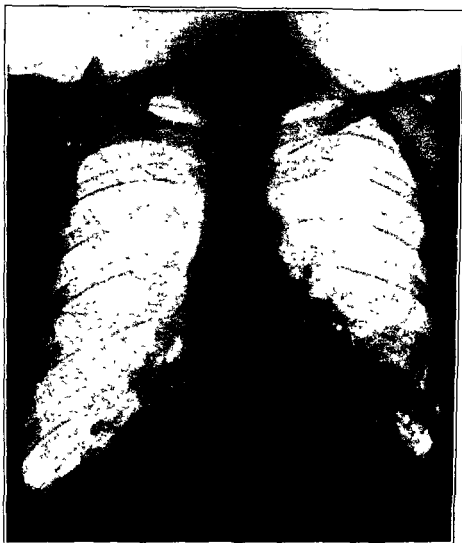


Fig. 11.—A male, 50 years of age, ill with a pulmonary infection involving both left and right lungs. Tubercle bacilli are not demonstrable though expectoration is copious. Diagnosis of tuberculosis questioned and further investigation of sputum revealed blastomycetes.

weight. Though he had a productive cough previously, at the time of admission he insisted that he did not expectorate. He was very toxic; his temperature ranged between 97°F and 103.6°F, and his pulse rate between 90 and 140.

On admission the patient appeared very ill. Physical examination and the roentgenogram disclosed extensive infiltration of the whole left lung which suggested a far-advanced stage of a caseous-pneumonic tuberculosis (Fig. 10). In

13 sputum examinations, 8 of which were concentrated, tubercle bacilli were not found. Because of the extensive disease and a repeatedly negative sputum the diagnosis of tuberculosis became questionable. A gastric lavage was performed and many tubercle bacilli were identified in the gastric contents.

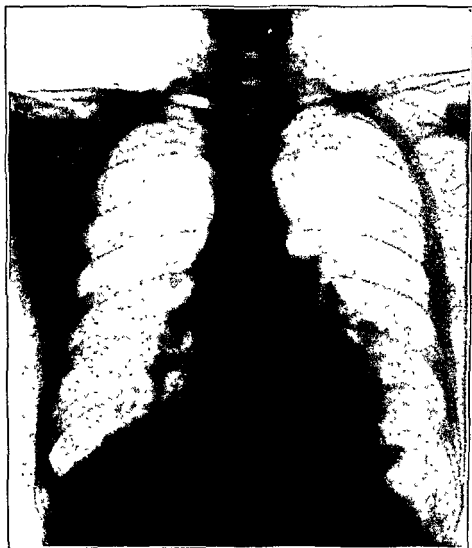


Fig. 12.—Diagnosis of blastomycosis is made in search for other organisms because of absence of tubercle bacilli in copious expectoration.

Whereas in the absence of expectoration, examination of the gastric contents may make the diagnosis, another good rule to follow is to question tuberculosis in the absence of tubercle bacilli with copious expectoration.

The following case report illustrates this rule:

CASE II.—A white male, 50 years of age, complaining of cough and expectoration with occasional blood-streaked sputum, was sent to the mountains for the treatment of pulmonary tuberculosis. While there, because of the profuse expectoration with the absence of tubercle bacilli, the diagnosis of pulmonary

tuberculosis was questioned. A careful study of the sputum was made for mycotic organisms. Blastomycetes were found in the sputum from which pure cultures of the fungus were grown. Injection of the culture into both rabbits and guinea-pigs produced blastomycosis. Figs 11, 12 and 13, are reproductions of the x-rays of this patient.

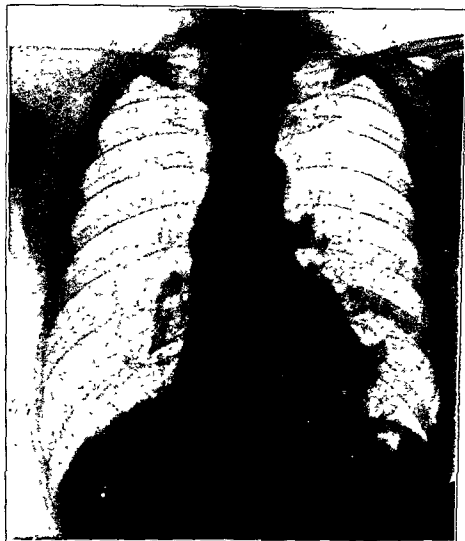


Fig. 13.—Disappearance of pathology in a case of blastomycosis following the use of ether per rectum

On the other hand repeated failures to find tubercle bacilli where expectoration is scant should not rule out the diagnosis of pulmonary tuberculosis. In chronic productive tuberculosis the infection is in the terminal bronchioles with involvement and atelectasis of the adjacent alveoli. When these small nodules caseate and ulcerate but few tubercle bacilli are discharged and their demonstration is difficult. The following case is an example of how misleading the repeated absence of tubercle bacilli may be:



CASE III.—A white male, 33 years of age, had been ill for three years. His illness started with gastric disturbances. He had a slight cough and expectoration. For two years he was treated for his gastric disturbances and finally an exploratory laparotomy was performed. His appendix was removed with no

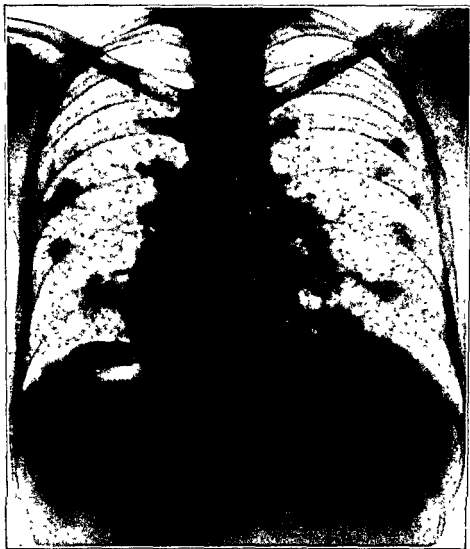


Fig. 14—A white male, 33 years of age, with extensive chronic productive tuberculosis and with over twenty examinations of sputum before tubercle bacilli were reported present. In scant expectoration negative demonstration of tubercle bacilli should not rule out tuberculosis.

relief of symptoms. Finally pulmonary disease was suspected and a roentgenogram revealed an extensive bilateral pulmonary tuberculosis. After a year at a sanatorium he decided to return home. At the tuberculosis center, because of sputum repeatedly negative for tubercle bacilli, a disseminated carcinomatosis was seriously considered. The patient reported to our Clinic on his return home. He complained of a distressing cough with slight expectoration. There were

diffuse, fine râles heard over both lungs. The roentgenogram (Fig. 14) revealed a disseminated nodular appearance of both lungs. His temperature was slightly increased and he had a rapid pulse between 90 and 120. In the past year he had lost twenty pounds. Twenty sputum examinations were reported negative for tubercle bacilli. The first sputum examination at the Clinic revealed tubercle bacilli and the diagnosis of *pulmonary tuberculosis* was sustained.

In scant expectoration negative demonstration of tubercle bacilli should not rule out tuberculosis.

### FISTULA IN ANO.

Though fistula in ano was formerly considered to be most often tuberculous in origin, the progressive advance in proctology has brought to light that tuberculosis plays only a small part in its etiology. Too often, however, the diagnosis of pulmonary tuberculosis is made months and years after the surgical treatment of fistula in ano when its mere existence should have made the surgeon suspicious of pulmonary tuberculosis.

### SYMPTOMS OF PULMONARY DECOMPENSATION.

In addition to the symptoms mentioned above, there is another group of complaints, not associated with pulmonary tuberculosis alone, but common to most all diseases of the lungs. We refer to the protean and ubiquitous manifestations of disturbances in *pulmonary physiology*. A complete discussion of this phase of symptomatology requires a thorough understanding of the physiology of respiration, the interchange and utilization of gases in tissue metabolism, and the whole correlation of these factors with the other systems of the human organism. Obviously this is beyond the scope of these brief remarks. Nothing can be attempted here other than to call the observer's attention to a few details which are sometimes apt to be overlooked. With the gradual encroachment of pathology on the normal lung tissue there occurs a gradual impairment of respiratory function. When this process extends over a considerable length of time, certain compensatory mechanisms are called into play which allow the individual to get along fairly well. Changes in the characteristics of the oxyhemoglobin dissociation curve, changes in the ability of the tissue so that it can utilize oxygen at a lower pressure, are but some of them. There comes a time, however, when these relief measures are inadequate. As might be expected, these symptoms of lung failure are noted first only on exertion. At rest the patient is quite comfortable. Later, with progressive disturbance of physiology, the means of compensation become increasingly inadequate so that even at rest the patient complains of embarrassment of respiration. Breathing may be rapid, heart palpitation may be noted, the patient is weak. When large areas of the lung are suddenly involved so that there is serious disturbance of pulmonary physiology, these compensatory mechanisms do not have sufficient time to be brought into play. As a result the patient will complain of all the symptoms of acute and severe lung failure. All too frequently these symptoms may be overlooked. They are of especial importance in the clinical care of the patient.

*Review.*—A careful review of the previous remarks will reveal the extreme importance of history taking in the diagnosis of pulmonary tuberculosis. As has been dramatically stated at various times, the fountain pen is one of the most valuable instruments in the diagnostician's armamentarium. For not only does the patient's recital focus the examiner's attention upon the particular system involved, which in the instance under discussion happens to be the respiratory system, but also does it give some clue as to the type of pulmonary pathology producing the symptoms. A brief consideration of tissue reaction in response to the stimulation of tuberculous antigen will readily show why this is so. In general, there are two main types of tissue response, the acute allergic and the slower relatively nonallergic type. A discussion of the factors producing the different tissue responses is given in the section on Classification to which the reader is referred for further details. As the pathogenesis of the process would suggest, the acute allergic types of reaction are explosive in onset. The symptoms therefore are apt to appear with dramatic suddenness and without any previous history of illness usually associated with chronic disease.

Because of the acutely toxic allergic reaction the symptoms of toxemia, besides appearing suddenly, are rather severe. The patient becomes very sick. The subsequent symptoms will depend entirely on the course of the pathology. In the benign exudative type where there has been a minimal amount of lung destruction, the allergic reaction soon subsides. Inasmuch as there has been no lung damage, there is no permanent pathology to prolong the symptoms. Therefore the short span of toxic symptoms and the few complaints due to the pathology in the lung itself soon give way to a perfect feeling of good health on the part of the patient.

In the caseous-pneumonic form, on the other hand, the acute symptoms are prolonged because of the nature of the underlying pathology. With the extensive necrosis that occurs, a toxemic allergic picture is produced which lasts far longer than that of the benign exudative type. Now the patient supplies his own tuberculous antigen in the form of caseous material and continues to do so until all of this has been sloughed out and expectorated. In order to accomplish this, cough and expectoration are profuse, depending, of course, on the amount of caseous material that must be sloughed away.

When the process has been completed, cough and expectoration diminish and the toxemic symptoms disappear because of the absence of any further antigenic stimulation. If the caseous erosion reaches a blood-vessel, hemorrhage may result. If the pleura is involved, pleural pain may be noted. Occasionally the erosion of the pleura occurs with such suddenness that adhesions do not have time to form. As a result a spontaneous pneumothorax is produced. This is apt to cause profound changes in lung ventilation with the result that the patient experiences considerable difficulty in avoiding serious anoxemia. Acute massive spreads of pulmonary pathology may cause similar pictures of pulmonary decompensation, especially before any compensatory mechanism of respiratory function sets in. Pain in the chest is more frequently present when the decompensation is due to pneumothorax than when acute pneumonia is the seat of the trouble. Thus, again, the history points the way.

In marked contradistinction to the acute forms, the relatively nonallergic type has none of the acute and sudden onset. Rather is it the long drawn out insidious affair which slowly but steadily progresses during the course of many years to reach a final crescendic climax before termination. The absence of allergic stimulation readily accounts for this. The slight cough or shortness of breath are due solely to the mechanical effects of the pulmonary pathology itself on lung physiology. Only rarely do slight toxic manifestations of allergic stimulation assert themselves. In the end-stage, however, when allergic reactions become very marked, fever, rapid pulse, anorexia and other toxic symptoms become very prominent. A clear understanding of this relationship between pathology and symptomatology will go far toward fathoming the perplexing depths of diagnosis.

### PHYSICAL EXAMINATION.

The next procedure in establishing the diagnosis is the physical examination. First, it is most important to bear in mind the fact that negative findings do not rule out pulmonary tuberculosis. We cannot emphasize too strongly that a physical examination of the lungs in which no abnormal changes are noted should not rule out tuberculous infection. In the past, many practitioners have been willing to eliminate the probability of this disease by physical examination alone. Physical signs are noted only when the pathology is close to the surface of the lung and is of a nature that can be detected by the examination. We will discuss the physical findings in their order of importance.

### AUSCULTATION.

One should be familiar with the normal changes in breath sounds over the thorax. In the right upper lobe broncho-vesicular breathing is heard because of the close proximity of the trachea. The broncho-vesicular sound varies in extent, usually being heard from the apex down to the first rib and sometimes as far down as the fifth rib anteriorly. The extent varies in different individuals, depending upon the proximity of the trachea to the right upper lobe. Because of this normal finding, many minimal lesions in the right upper lobe are overlooked. It is most difficult to differentiate a minimal tuberculous infiltration from normal broncho-vesicular breathing. In the apex of the right axilla vesicular sounds are heard normally.

Ornstein,<sup>7</sup> in 1925, brought attention to the fact that broncho-vesicular breathing heard in the apex of the right axilla is almost pathognomonic of a tuberculous involvement in the upper lobe. The absence of broncho-vesicular breathing in this area, however, does not rule out the possibility of pathology. When broncho-vesicular breathing is heard in the right upper lobe but with no history suggesting pulmonary pathology, tuberculosis may be ruled out in that location. On the other hand, a history pointing to the possibility of tuberculous infection, together with broncho-vesicular breathing in the right upper lobe should be construed in favor of tuberculosis until diagnosed otherwise.

Broncho-vesicular breathing in the left upper lobe may be considered almost pathognomonic of pulmonary tuberculosis. The old Krause law which stated

that pathology in the upper lobes is to be considered tuberculous and pathology in the lower lobes nontuberculous until proven differently, should be disregarded. In large cities it is very common to find tuberculosis infecting any lobe. Basal tuberculous disease is not as uncommon as has been regarded in the past.

Another important finding in pulmonary tuberculosis is the presence of *moist mucous râles*. When they are heard with normal quiet breathing, one may be sure that the process is moderately or far-advanced. On the other hand, if râles are not heard with the quiet breath sounds, they may be brought out in the following manner. The patient is made to breathe deeply, exhale, cough, and then take a deep inspiration. Should râles be heard, they are termed "*latent râles*." When heard over the upper lobes, tuberculosis should be immediately considered. Moist râles are not always elicited in tuberculosis of the lungs. In an investigation of a large series of cases at one of our clinics we found that in over 40 per cent. of the cases no râles were heard. Therefore, one must not depend entirely upon the presence of moist râles in establishing a diagnosis of tuberculosis.

Another important physical sign in the diagnosis of tuberculosis is the presence of *vicarious emphysema* over one lobe or lung. If in one lung there is extensive disease, vicarious emphysema is heard over the opposite lung. No attention need be paid to this vicarious emphysema. On the other hand, if this exaggerated vesicular sound is heard over one lung with no evidence of disease in the contralateral one, one should be suspicious that a central infection may be the reason for this compensation. Therefore, unilateral compensatory emphysema over one lung is an excellent lead in the diagnosis of central tuberculosis in that lung.

### PERCUSSION IN DIAGNOSIS.

The percussion note is very important as an aid in the diagnosis of minimal tuberculous lesions. One must remember that changes in the thoracic contour may lead one astray. Again, it must be kept in mind that the right upper lobe percusses dull normally. This is accounted for by the following reasons: *First*, the muscular development is usually on the right side of the thorax; *second*, the right upper lobe is small in volume compared with the left upper lobe; *third*, the large vessels of the neck run slightly anterior to the right upper lobe. The percussion stroke should be very light. When the percussion stroke is heavy, deep portions of the lung are vibrated and the superficial areas that may give the change to the note with light percussion are overlooked. Any change in the pitch of the percussion note should make one suspicious of changes in lung tissue. Except in extensive lesions, tactile fremitus is apt to be of little help.

Again the fact must be emphasized that only positive physical findings are of any importance. Changes in breath sounds, frequently associated with the appearance of moist râles, should be interpreted as probable evidence of pulmonary tuberculosis, especially where there is a history suggesting pulmonary disease.

## X-RAY EXAMINATION.

The roentgenogram is the most valuable aid in the diagnosis of pulmonary tuberculosis. The x-ray rarely fails to demonstrate the disease in the lungs. Failures occur when the tracheobronchial lymph glands are involved. The



Fig. 15.—An apparent negative x-ray for pulmonary tuberculosis. The patient had a positive sputum for tubercle bacilli. A bronchoscopic examination revealed a tuberculous disease of the left main bronchus and the bronchus leading to the left lower lobe.

failure is due to merging of these shadows with those of the mediastinum. With involvement of the above glands the large bronchi may be infected and tubercle bacilli expectorated from the walls of the bronchi. In such a case we may have negative roentgen findings and positive sputum (Fig. 15).

When the tuberculous pathology occurs in those portions of the lung bordering on the mediastinum, the shadows may also be masked.

X-ray technic is important. Over-penetration should be frowned upon. The usual x-ray examination should consist of three exposures: one in the posterior-anterior position, a second in the anteroposterior position, and a third in the oblique position, preferably the second oblique in which the left shoulder is close

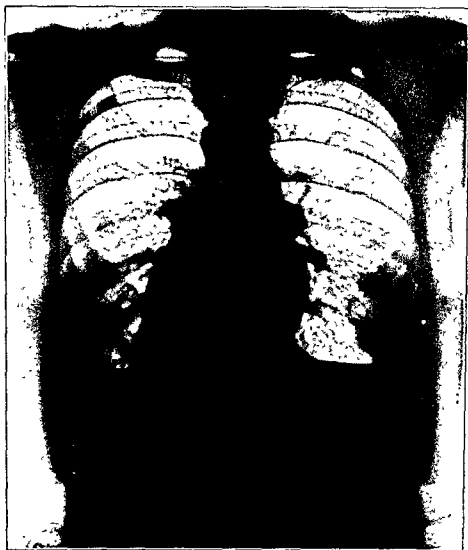


Fig. 16—A posterior-anterior x-ray of the thorax of an adult female complaining of cough, expectoration and hemoptysis, which disclosed no evidence of clinical pulmonary disease. An oblique position, Fig. 17, however, accounted for the symptoms.

to the plate and the right shoulder away. Failure to take the oblique view may leave uncovered pathology in the lung field behind the cardiac shadow or densities in the mediastinum or retrocardiac space. The following case illustrates this point.

CASE 1.—Female, 29 years of age, married, mother of two children, came in for an examination because of a persistent cough with expectoration. She fatigued easily. Occasionally the sputum was streaked. One year ago she had

hemoptysis of more than two drams. Physical examination revealed scant physical findings except for a suggestion of interference of the movement of air into the bronchial tree and diminished intensity of breath sounds in the right lower lobe. A few inconstant sibilant râles were heard over this lower lobe.



Fig. 17.—An oblique position in which the heart and mediastinum are cast into the right thorax to visualize the mediastinum and the tracheo-bronchial tree, demonstrates that the main bronchus and the bronchus to the right lower lobe are engulfed in a mass of calcified glands causing a bronchiectasis which accounts for both the hemoptysis, cough and expectoration.

The left lung was normal. X-ray examination (Fig. 16) posterior-anteriorly showed no lung parenchymal involvement. There was an obliteration of the costophrenic angle on the right side due to an old pleurisy. The diaphragm was rather flat, probably due to this old pleural reaction. The mediastinal shadow was irregular along the right border with bulging out in the right thoracic



space. There was no evidence of any tuberculous disease. Except for marked accentuation of all the bronchial markings throughout both lungs, the lungs could be considered normal. It was difficult from this posterior-anterior x-ray to account for her cough and expectoration. The physical signs suggested some pressure on the bronchus leading to the right lower lobe and a second oblique picture was taken (Fig. 17). In this oblique position one can visualize the trachea and its bifurcation. A glance along the right main bronchus shows that the right main bronchus and its branches are engulfed in a mass of calcified glands. Because of this pressure along the right main bronchus, there is a bronchiectasis. The hemoptysis, the cough and the expectoration are all secondary to enlarged bronchial lymph glands adjacent to the right main bronchus. If this picture had not been taken in the left oblique position, a diagnosis could not have been established.

We wish to impress the reader with the fact that the x-ray, though important in itself, cannot definitely substantiate the diagnosis of tuberculosis. History-writing and physical examination are equally as important inasmuch as the patient is brought to the point of being x-rayed because of these examinations.

### LABORATORY EXAMINATION.

The importance of the *examination of the sputum* cannot be over-emphasized. How frequently this phase of the examination is not carried out is surprising. Quite often cases are referred to tuberculosis institutions with a diagnosis of pulmonary tuberculosis, not even one sputum examination for tubercle bacilli having been made. The finding of tubercle bacilli in the sputum is the most definite evidence of tuberculosis. We have previously discussed the importance of examination of the gastric contents in patients who do not expectorate and who show definite pathology in the x-ray.

No examination for tubercle bacilli is complete unless there has finally been a gastric lavage and an examination of the stomach contents for tubercle bacilli. *We have noted that the best period for the removal of the gastric contents is when the patient awakens in the morning.* We also wish to re-emphasize what has been previously said concerning the large amount of expectoration in the absence of tubercle bacilli. One should then begin to search for some other etiological factor. Where there is scant sputum, repeated negative examinations for tubercle bacilli should not rule out the diagnosis of tuberculosis.

*Summary.*—In summarizing the important factors in establishing a diagnosis are readily seen to be dependent upon more than any one examination. It is dependent on a combination of modes of examination, one as important as the other. The history may be the first lead to the diagnosis. The physical examination in itself is only of value when the findings are positive. The x-ray is very important and the finding of tubercle bacilli in the sputum is most conclusive. Frequently all forms of examination must be used to finally make the diagnosis of pulmonary tuberculosis.

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## CHAPTER IX.

# CLASSIFICATION OF PULMONARY TUBERCULOSIS.

GEORGE G. ORNSTEIN AND DAVID ULMAR.

**Pathogenesis.**—The many classifications of pulmonary tuberculosis that have been written have depended almost entirely on the pathologic impressions at the end stage of disease. At the postmortem table there is such a variegated picture of pulmonary tuberculosis that a clear concept and a workable classification of the dynamic pulmonary tuberculosis seems hopeless. Another disturbing element is the attempt to classify pulmonary tuberculosis as it occurs in childhood differently than in adults. If this were true, the tubercle bacillus would then have to produce various manifestations of disease at different age periods. This seems improbable. A study of the pathogenesis of pulmonary tuberculosis associated with clinical observations through the course of the disease and aided by serial x-rays has helped clear up the situation.

Clinical pulmonary tuberculosis is the same at all ages. Confusion can be avoided if the term "childhood tuberculosis" is omitted. Following the primary infection all reactions in the lung depend upon the sensitivity of tissues and the dose and virulence of the tubercle bacilli. The term "childhood tuberculosis" has been given to the train of phenomena that follows the first implantation of tubercle bacilli. Parrot<sup>1</sup> and his pupil, Kuss,<sup>2</sup> stressed the importance of this primary infection. Unfortunately their work was forgotten. Years later it was brought to light by Albrecht<sup>3</sup> and Ghon.<sup>4</sup> The latter has ably described the anatomical picture of this first infection. Because of Ghon's repeated confirmation and classical descriptions of this primary infection, his name has been associated with the peculiar anatomical formation.

When the infection occurs through the respiratory tract, it begins as an exudative, rapidly caseating bronchopneumonic focus which stands out sharply against the surrounding lung tissue. There is a similar but larger reaction in the related lymph node. The infection occurs in the lung parenchyma, usually just under the pleura. This exudative rapidly caseating bronchopneumonic patch varies in size and may occur in any part of the lung, usually in the upper lobes. As a rule it is single but may be multiple. The infection spreads through the lymph to the regional lymph node where a similar but larger reaction occurs. This primary lesion not only tends to calcify but also to ossify.

Puhl,<sup>5</sup> in 1922, besides confirming the picture of primary infection as described by Ghon, also pointed out the peculiar mode of healing by calcification and tendency to ossification. Puhl<sup>6</sup> states that the ossification may occur in reinfection. He also states that though it may occasionally occur in reinfection the occasion is so infrequent that ossification should be looked upon as representing healed primary infection. The parenchymal infection with the related regional lymph node is called the primary affect or primary complex.

*Superinfection.*—Following the primary affect the response of the body tissue to tubercle bacilli is different than at the time of the first infection. As Koch<sup>7</sup> pointed out in his experiments on reinfection in guinea-pigs, the superinfection takes only a few hours to manifest itself (Koch phenomenon). The reaction is both acute and inflammatory. This sensitivity to tuberculous antigen has frequently been called allergy. So, in humans, the superinfection immediately following the primary affect is acute and exudative. We now understand the acute exudative spreads that frequently occur in children. The superinfection may be either exogenous or endogenous. The reaction depends a great deal on the dose of tubercle bacilli. The superinfection may come from the primary bronchopneumonic focus in the lung or from the related caseous regional lymph nodes.

Frequently these endogenous superinfections are the cause of extensive exudative forms of tuberculosis so often seen in childhood. This superinfection is quite different from the first infection in that there is localization of bacilli at the site of inoculation and no migration of organisms to the regional lymph nodes as is so characteristically seen in the primary affect. Also one must begin to consider seriously whether this increase in tissue sensitivity is a protection or a detriment to our resistance to tuberculosis.

*Infection.*—In adults, where the primary infection has taken place and healed, the result of the superinfection is dependent a great deal on two factors, the sensitivity of the tissues and the infecting dose of tubercle bacilli. Infection in adults is chiefly exogenous. Our clinical experience points towards such a mode of infection. The tuberculosis death rate is highest amongst peoples where hygienic conditions are deplorable and especially where there is overcrowding.

Endogenous infection occasionally occurs in adults. A tracheal, bronchial or bronchopulmonary gland may rupture and its contents be aspirated into the lung. This, however, is not the common mode of infection. Surely we must forget the teachings of Von Behring<sup>8</sup> that adult tuberculosis is the end stage of an infection in childhood.

One must be careful then not to accept the pathogenesis of adult tuberculosis as similar to the pathogenesis in early life as presented by the pathologist. The pathogenesis is different than that of the primary affect where there may be rapid superinfection due either to bronchogenic dissemination of caseous material from the broken-down caseous "primary affect" or to hematogenous dissemination following rupture of the focus into a blood-vessel. In adults, clinical pulmonary tuberculosis, as has been pointed out, begins long after the primary affect has calcified. How great a rôle the primary affect plays in adult infection is not definitely known. Its importance will depend on the effect it has had on the sensitivity of the tissue to tuberculous antigen. The clinical forms of pulmonary tuberculosis are determined a great deal by this resulting tissue sensitivity. Of equal importance, however, is the dose and virulence of the superinfecting tubercle bacilli. Upon the interrelation of these various factors will be determined the resultant clinical tuberculosis, a tuberculosis which may be roughly divided into two main types: (I) exudative, and (II) productive.

## I. THE EXUDATIVE REACTIONS.

The exudative reactions are characterized by high tissue sensitivity to tuberculous antigen so that there is an immediate and explosive reaction whenever the tissue of the host comes in contact with tubercle bacilli. The extent of the cell irritation that occurs will be dependent upon the mass or concentration of the irritant bacilli, the greater the mass or dosage the more likely the opportunity for overirritation and resultant cell death. On the basis of these reactions the exudative form of tuberculosis may be divided into two main types, a type that grossly resolves and a type that does not resolve but rather leads to lung destruction. The resolving type we have separated into two clinical entities, a very rapidly clearing benign exudative form, and a slower resolving exudative-productive form. The nonresolving type we have termed caseous-pneumonic tuberculosis.

### RESOLVING EXUDATIVE TUBERCULOSIS.

**Benign Exudative.**—Because of great tissue sensitivity, contact with a small amount of tubercle bacilli produces an exudative form of reaction. The response is chiefly serous with little fibrin and a small amount of cellular element. There is little or no resulting death of tissue. The exudate is absorbed and the patient becomes well in a short space of time without leaving in the roentgenogram any visible trace of the previous infection.

**Exudative-Productive.**—With similar high tissue sensitivity but a larger dose of tubercle bacilli the reaction is more violent. Besides the serous exudate there is more fibrin and a great deal of cellular element. Fortunately there is comparatively little resulting death of tissue. The exudate is again absorbed. After a longer period of time the patient becomes well again. Serial x-rays show a complete resolution of the exudate except for a few small areas of productive changes and an occasional fibrotic strand.

### NONRESOLVING EXUDATIVE TUBERCULOSIS.

**Caseous-pneumonic.**—Here in addition to a high tissue sensitivity there is a large dose of tubercle bacilli. The reaction is severe with a resultant death of tissue. There is caseation and necrosis. Following liquefaction of the whole mass the dead tissue is sloughed out with the resulting cavity formation that characterizes this form of tuberculosis. From the walls of these cavities tubercle bacilli are constantly shed and are a source of supply for superinfection. These patients are a constant threat to themselves, their families and their associates. They swallow large numbers of tubercle bacilli so that tuberculosis of the intestinal tract and the larynx are frequent complications. To this form of pulmonary tuberculosis the term "malignant" has been applied.

## II. THE PRODUCTIVE FORM OF TUBERCULOSIS.

When the tissue sensitivity is low and the dosage of tubercle bacilli is small, the response is productive rather than exudative. The infection begins in the terminal bronchiole and invades the surrounding mucous membrane. As a

result of this infection there follows an obliteration of the bronchus with an atelectasis of the terminal portion of the lung. The alveoli then become involved. The reaction is cellular. There is typical tubercle formation with epithelioid and giant cells and fibroid changes. Aschoff<sup>9</sup> called this form of tuberculosis acinous productive tuberculosis. Because of the avascularity, the lesions may break down and ulcerate into the smaller bronchi. Tubercle bacilli are then aspirated into adjacent portions of the lung. Infection now takes place through the small bronchi, the process slowly browsing down through the lung. Frequently the opposite lung becomes involved. The process begins in the apex and slowly descends. When extensive it may have the appearance of a blood-stream infection. We have termed this form of pulmonary tuberculosis "chronic-productive tuberculosis." The course is usually very slowly progressive. It most frequently manifests itself in the advanced stages. This productive form of tuberculosis takes about twenty years to involve both lungs.

The above classification is a qualitative classification described by Ornstein, Ulmar and Dittler<sup>10</sup> in 1930. It differs considerably from most classifications which are usually dependent upon extent of disease and symptoms.

The following is the classification adopted by the American Sanatorium Association and by the National Tuberculosis Association.

## CLASSIFICATION OF ADULT TYPE OF TUBERCULOSIS.

### SCHEMA FOR THE CLASSIFICATION OF PATIENTS ON EXAMINATION

#### I. *Minimal Lesion.*

(a) Slight infiltration without demonstrable excavation.

(b) A small part of one or both lungs—Total volume of involvement, regardless of distribution, shall not exceed the equivalent of the volume of lung tissue which lies above the second chondrosternal junction and the spine of the fourth or body of the fifth thoracic vertebra on one side.

#### *Symptoms:*

1. Slight or None.

Slight or no constitutional symptoms, including particularly gastric or intestinal disturbance or rapid loss of weight; slight or no elevation of temperature or acceleration of pulse at any time during the 24 hours. Expectoration usually small in amount or absent. Tubercle bacilli may be present or absent.

2. Moderate.

No marked impairment of function, either local or constitutional.

3. Severe.

Marked impairment of function, local or constitutional.

#### II. *Moderately Advanced Lesion.*

Lesion allowable under Moderately Advanced—one or both lungs may be involved, but the total involvement shall not exceed the following limits:

(a) Slight disseminated infiltration or fibrosis which may extend through not more than the equivalent of the volume of one lung.

(b) Severe infiltration, with or without fibrosis, which may extend through not more than the equivalent of one-third the volume of one lung.

(c) Any gradation within the above limits.

(d) Total diameter of cavities, if present, should not exceed 4 cms. (see Technical Procedures).

*Symptoms:*

1. Slight or None.

Slight or no constitutional symptoms, including particularly gastric or intestinal disturbance or rapid loss of weight; slight or no elevation of temperature or acceleration of pulse at any time during the 24 hours. Expectoration usually small in amount or absent. Tubercle bacilli may be present or absent.

2. Moderate.

No marked impairment of function, either local or constitutional.

3. Severe.

Marked impairment of function, local or constitutional.

*III. Far Advanced Lesion.*

A lesion more extensive than under Moderately Advanced. Or definite evidence of greater cavity formation.

*Symptoms:*

1. Slight or None.

Slight or no constitutional symptoms, including particularly gastric or intestinal disturbance or rapid loss of weight; slight or no elevation of temperature or acceleration of pulse at any time during the 24 hours. Expectoration usually small in amount or absent. Tubercle bacilli may be present or absent.

2. Moderate.

No marked impairment of function, either local or constitutional.

3. Severe.

Marked impairment of function, local or constitutional.

SCHEMA FOR THE CLASSIFICATION OF SUBSEQUENT OBSERVATIONS.

1. Apparently Cured.

All constitutional symptoms absent; sputum, if any, microscopically negative for tubercle bacilli; x-ray findings compatible with a healed lesion. These conditions shall have existed for a period of two years under ordinary conditions of life.

II. Arrested.

All constitutional symptoms absent; sputum, if any, microscopically negative for tubercle bacilli; x-ray findings compatible with a stationary or retrogressive lesion. These conditions shall have existed for a period of six months, during the last two of which the patient has been taking one hour's walking exercise twice daily or its equivalent.

III. Apparently Arrested.

All constitutional symptoms absent; sputum, if any, microscopically negative for tubercle bacilli; x-ray findings compatible with a stationary or retrogressive lesion. These conditions shall have existed for a period of three months, during the last two of which the patient has been taking one hour's walking exercise twice daily or its equivalent.

## IV. Quiescent.

All constitutional symptoms absent; sputum, if any, microscopically negative or positive for tubercle bacilli; x-ray findings compatible with a stationary or retrogressive lesion. These conditions shall have existed for a period of two months, during the last month of which the patient has been taking one half hour's walking exercise twice daily or its equivalent.

## V. Improved.

Constitutional symptoms lessened or entirely absent; sputum, if any, microscopically negative or positive for tubercle bacilli; x-ray findings to be those of a stationary or retrogressive lesion.

## VI. Unimproved.

Essential symptoms unabated or increased; x-ray findings to be those of an active or progressive lesion.

## VII. Died.

## SPECIAL PROVISIONS AND DEFINITION OF TERMS.

Physical signs and x-ray findings are often at variance, and a given lesion should be classified by the method revealing the greater extent or intensity.

It should be made clear that x-ray findings may be definite where physical signs are negative or doubtful, or, less frequently, that definite tuberculosis may exist without demonstrable x-ray change.

Induced pneumothorax or nonpulmonary complications should not influence classification but should be recorded with the classification.

## 1. Marked Impairment of Function.

(a) *Local*—marked dyspnea on exertion, limiting seriously the patient's activity.

(b) *Constitutional*—marked weakness, anorexia, tachycardia.

The above classification is based almost entirely upon extent of pathology measured by physical signs or by the roentgenogram. To it is added the symptoms of the patient. It recognizes no quantitative changes.

We have merged the above two classifications and now have both a qualitative and quantitative measure of the disease. For example, when one describes a far-advanced lesion, it may be benign exudative, benign exudative-productive, malignant caseous-pneumonic, or chronic productive. The benign exudative, the exudative-productive and chronic productive would give an entirely different prognosis than the far-advanced caseous-pneumonic tuberculosis. In the benign forms of exudative tuberculosis one could with certainty state that the patient probably will get well, whereas in the far-advanced caseous-pneumonic or chronic productive tuberculosis one would be very hesitant concerning the prognosis. A minimal stage caseous-pneumonic tuberculosis would warrant a bad prognosis, whereas in a far-advanced benign exudative lesion, the prognosis would be good. We can therefore readily understand the importance of a qualitative classification.

Aschoff's<sup>11</sup> pathological classification may be adopted as a clinical classification. This classification is based on the type of reaction, the localization and the extent of the infection. Aschoff divides it into two important groups: (1) productive phthisis and (2) exudative phthisis.



## 1. PRODUCTIVE PHTHISIS.

(A) Acinous productive phthisis.

(B) Acinous nodose phthisis (through the fusion of individual acinous fossi to the size of the cherry or still larger nodules).

(C) Cirrhotic phthisis (more widely confluent acinous nodose fossi with diffuse shrinking of the entire cicatricial lung areas).

## 2. EXUDATIVE PHTHISIS.

(A) Acinous exudative processes.

(B) Lobular caseous phthisis.

(C) Lobar caseous phthisis.

The origin of A and B under Exudative Phthisis is similar to that of A and B under the productive form, namely, the fusion of acinous fossi. According to the site, mention is made of apical cranial or caudal localization. A case may be designated as apical, cavernous, cranial-acinous nodose, or caudal acinous productive phthisis.

As stated previously, this is chiefly a pathological classification. It can be immediately seen that there is no place for those types of pulmonary tuberculosis that resolve, namely, the benign exudative and the exudative-productive forms. Had Aschoff placed these two important forms of pulmonary tuberculosis in his classification there would have been no need for any attempt at further clinical classification of pulmonary tuberculosis.

On the pages to follow will be described in greater detail the benign exudative, the exudative-productive, the caseous-pneumonic and the chronic productive types mentioned above.

## BENIGN ACUTE PULMONARY TUBERCULOSIS.

**History.**—The conception of tuberculosis as an acute disease is not new. The French School was probably the originators of the idea, there being mention made as early as 1829. Grancher<sup>12</sup> in 1877 described a splenopneumonic tuberculeuse, but his ideas do not seem clear. It is really not till the present century that any definite views have been published as to the acute form of tuberculosis. Thus, Bard,<sup>13</sup> in 1901, in his classification, viewed this splenopneumonic of Grancher as a form of the true caseous pneumonia.

In a lecture on the curability of acute phthisis Anderson,<sup>14</sup> in 1890, said that its prognosis was not gloomy. He cited the case of a man who was well after an illness of 28 days. In 1906 West<sup>15</sup> divided acute phthisis into two groups. He stated that "both are attended with extensive inflammatory consolidation but in one, consolidation itself is tuberculous, for tubercle bacilli are found in the alveolar contents and it rapidly caseates; in the other, the consolidation is simply inflammatory and not really tuberculous. It may resolve and then disappear." Heller,<sup>16</sup> in 1904, and Hedinger,<sup>17</sup> in 1906, published the autopsy reports of extensive acute lobar tuberculosis where the process had not extended to caseation. It was their idea, however, that if the patients had lived long enough caseation would have occurred. In 1909 Gerhardt<sup>18</sup> cited an acute case

with recovery in 13 weeks and complete well-being one year later. He stressed A. Fraenkel's<sup>19</sup> point of the resorbability in the gelatinous area where no tubercle bacilli were to be found. In the following years Bezancon and Braun<sup>20</sup> and Mohr-Stahelin<sup>21</sup> pointed to the disappearance of acute infiltrations.

In this country it was Wessler<sup>22</sup> who first published the roentgenological disappearance of large consolidations, but he did not conceive the lesion to be benign for he speaks of these patients having "wavered on the brink of death." In 1925 Redeker<sup>23</sup> described the disappearance in children of extensive tuberculous processes in a short time. A similar process in adults was described in 1926 by Fassbender<sup>24</sup>. Thirty-one cases were cited. Fleischner,<sup>25</sup> in 1925, described the rapid disappearance of exudative processes, which on x-ray could not be differentiated from the nonresorbable caseous pneumonic type. In 1926 Sergent and Durand<sup>26</sup> stated there was a lobar form of tuberculosis which resorbs completely. Rist in 1916<sup>27</sup> and again in 1929,<sup>28</sup> speaks of an acute form of tuberculosis which may recover rapidly. To continue with this review of the literature would be repetitious.

The following men have contributed to the study of an acute form of tuberculosis: in 1920, Elhasberg and Neuland<sup>29</sup>; in 1921, St. Engel<sup>30</sup>; in 1922, Assmann,<sup>31</sup> Jaquero<sup>32</sup>, Armand-Delille,<sup>33</sup> and Klinkert<sup>34</sup>; in 1923, Schurmann,<sup>35</sup> Harms,<sup>36</sup> Piquet and Giraud<sup>37</sup>; in 1926, Ulrici,<sup>38</sup> Bacmeister,<sup>39</sup> Ickert<sup>40</sup> and Lydtin<sup>41</sup>; in 1927, Crecelius,<sup>42</sup> Lindig<sup>43</sup> and Neumann,<sup>44</sup> Romberg<sup>45</sup> and Jacob<sup>46</sup>; in 1928, Brecke,<sup>47</sup> Alexander<sup>48</sup> and Mastbaum<sup>49</sup>; in 1929, McPhedran<sup>50</sup> and in 1931, Ornstein, Ulmar and Dittler.<sup>51</sup>

**Etiology and Pathology.**—Concerning the pathology of this type of tuberculosis, very little is definitely known, for the simple reason that patients with this form of tuberculosis do not die but usually recover. The reaction that is seen is dependent upon the peculiar effect the primary infection has upon the tissue of the host. As a result of the initial inoculation there is found in certain individuals a very marked sensitivity to tuberculous antigen. Any stimulation of this sensitivity response will provoke a sudden intense irritation of the tissue with a resultant exudative reaction. If the amount of aspirated tuberculous material is small so that the irritation of the lung tissue is not excessive, there will occur this sudden, more or less massive, exudative affair in the lung parenchyma with very little or no actual demonstrable lung destruction. If the same individual is then removed from the source of bacilli so that there will be no further dosage to cause permanent damage, then the acute exudative reaction will subside, the exudate will be absorbed, and no trace of the previous pathological changes will remain.

From this brief discussion it can be seen how significant becomes the history of contact with an open case of tuberculosis. An allergic individual inhales a dose of tubercle bacilli that has been sprayed out by a person with a positive sputum. The bacillary protein comes in contact with the highly sensitized lung tissue. A tremendous exudative reaction takes place—practically similar to the tuberculin reaction (Koch phenomenon). There is a tremendous serous exudation into the alveolar walls and alveoli, a slight amount of fibrin, and just a few cells. The few bacilli which were the cause of the reaction soon become "lost in

the scuffle," so to speak, and eventually disintegrate and are destroyed. It is therefore difficult to find the bacilli in the sputum and after the first few days of the illness they are practically never seen. This is the type of reaction that is found when the dosage of bacilli is derived from an exogenous source.

A similar picture may result when the germs are derived from an endogenous source, that is, when the organisms spill over from one part of the lung field and set up an exudative focus in some new area. There are also times when a tremendous exudative reaction takes place about an old proliferative focus. The exact pathogenesis of this reaction is not quite clear. One thing, however, is certain, and that is that allergic tissue has been stimulated to reaction by tubercle-bacillus protein. With the removal of the irritating stimulus or possibly a raising of the threshold of stimulation, the process resolves, leaving the original slight scar. The characteristic feature of the reaction, whatever the source of infection, is the tremendous exudative or serous response, with very little cellular and proliferative or fibroid change.

**Symptomatology.**—The symptoms presented by patients with this type of pathological involvement are typically very slight. Usually the disease is ushered in by what is described as an ordinary every-day cold. Following a period of perfect health, the patient, generally a young adult in the authors' series, although this type of reaction may occur at any age, notices the onset of a slight cough. This cough, never severe, within a few days to a week diminishes, so that by the end of a week or so the patient is coughing practically not at all. Coincident with the onset of the cough there is a scanty amount of sputum. This expectoration lasts but a few days and then disappears. This fact is of great practical significance. If tubercle bacilli are to be found in the sputum, they must be searched for within the first few days of the onset of the disease. Subsequent examinations may be made on ordinary saliva furnished by an obliging patient who is unable to raise any sputum. At the onset of the attack, the patient may feel a trifle below par. This feeling of malaise and lassitude may be no greater than that associated with an ordinary common cold. It soon disappears, and with the subsidence of the cough and expectoration the patient feels perfectly well. The entire symptom-picture usually lasts no longer than a few days to a few weeks, and, as far as the patient himself is concerned, he is willing to consider himself cured by the end of this short period.

In this description of the symptomatology there is one finding which has not been mentioned up to now. When present it is of very great significance and serves to differentiate this type of pulmonary infection from that found in the common cold. This is the symptom hemoptysis. Blood-spitting has been noted in 43 per cent. of our series. When present, it occurs at the very onset of the disease. It may vary in amount from merely blood-streaked sputum to copious hemorrhage of a pint or more. The authors know of no ordinary cold which produces this picture. When hemoptysis is associated with a slight cough and expectoration which soon disappear and leave the patient feeling perfectly fit, one should be very suspicious of the presence of the acute benign form of pulmonary tuberculosis. If the patient gives a history of recent contact with an open case of tuberculosis, the diagnosis is practically clinched.

**Physical Signs.**—The physical signs in this type of disease are surprisingly scant when one considers the extent of the pathological changes as revealed by the x-ray. Usually the breath-sounds over the involved area are markedly diminished; in fact, their intensity is diminished to such an extent that the quality of the breathing occasionally cannot be determined. When the type of respiratory murmur can be distinguished, it is usually found to be bronchovesicular. At the onset of the disease there may be a few fine high-pitched moist râles scattered over the involved area. These râles, never numerous, seldom coarse, usually fine and high-pitched, persist for a varying length of time. They may be present for but two or three days and then completely disappear. In other cases, they may be heard for the duration of the pathological process. Sometimes there are a few scant sibilant or sonorous râles. Occasionally no râles are ever heard. There is one finding, however, which is fairly constant. Dullness on percussion can usually be obtained over the involved region, provided that the area is extensive enough and sufficiently close to the chest wall to be revealed by this method of physical diagnosis. When one considers the exudative nature of the process, one is not at a loss to explain the paucity of physical signs. The edematous water-logged alveolar walls act as perfect felt-pad dampers and thus prevent the formation or transmission of breath-sounds or râles. The percussion note, however, is not influenced by this factor and is therefore dull.

**X-rays.**—Following upon a somewhat unimpressive history and very scant physical signs, the x-ray film is rather astounding. In full bloom the roentgenographic picture presents a dense homogeneous shadowing. This shadow may be of any size and may occupy any portion of the lung field. Frequently it involves an entire upper lobe, and when on the right side may have a sharp lower border at the level of the interlobar fissure between the upper and middle lobes. Occasionally the shadow is wedge-shaped with the base toward the periphery of the lung field and the apex toward the hilum. Extensive as the x-ray shadowing may be, it is very rapid in making its appearance. One of our cases showed marked changes within four days. The first change to be noted is a diffuse haze and impairment of illumination over the involved area. This is followed by a rapid increase in the density of the shadow, until the typical homogeneous opacity is obtained.

Once the peak of the reaction has been reached and the process tends to resolve, the x-ray shadow tends to disappear. This it does in one of two different ways. The shadowing may gradually disappear by means of a uniform diminution of the density—a reversal of its formation. The more usual manner of disappearance is by means of an irregular absorption of the shadowing, leaving mottled patchy appearance, exceedingly suggestive of cavitation. This absorption may even take place in such a manner that the entire center of the shadow is absorbed, leaving a large area of high light which is usually diagnosed by the roentgenologist as a large cavity. At other times this irregular fade-out may, in the course of its resolution, present an appearance similar to the shadowing caused by the chronic proliferative or acinous type of tuberculosis. Serial x-rays, however, often after a period of no longer than six weeks to a few months, show that the entire shadowing disappears, usually without leaving a

trace. It is very important that these x-ray shadows be recognized during their stage of resolution. Frequently the patient is seen late in the course of the disease and only after the lesion has been discovered during routine fluoroscopic examination. Unless one is cognizant of the peculiar irregular process of absorp-

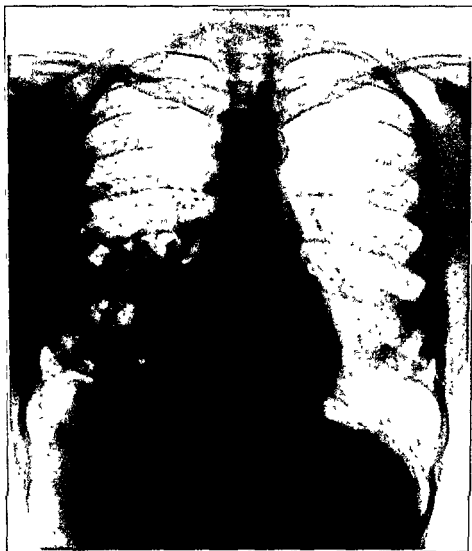


Fig 18.—An x-ray of a young female (Case No. 1) with an exudative tuberculosis in the lower half of the right lung. The disease is in the process of resolution.

tion of the shadow, the case may be diagnosed as advanced tuberculosis with cavity formation

**Sputum.**—The sputum in these cases, at no time very copious, very quickly disappears so that within a few days to two weeks the patient is coughing not at all. Therefore if bacilli are to be found, they must be searched for at the very onset. They are never numerous and soon disappear completely. This is in marked contrast to the other acute forms of tuberculosis and forms one of the distinguishing characteristics of the acute benign type.

**Treatment.**—Once the diagnosis of benign acute exudative tuberculosis has been made, the prime essential of treatment consists in leaving the patient alone and not interfering with resolution which will normally take place spontaneously. In fact, it is quite conceivable that meddling treatment may interfere with the normal rapid resolution. There is one tenet of treatment, however, which

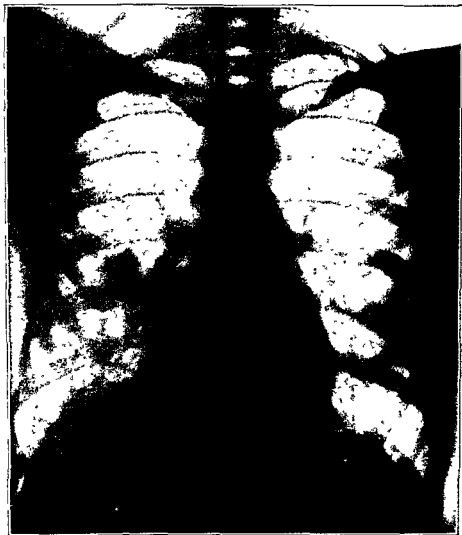


Fig. 19—X-ray of Case No. 1 showing the extent of resolution after 41 days. The annular shadow has disappeared.

must be rigidly observed. These patients, being hypersensitive to tuberculous antigen, must be carefully protected from contact with the open case. To them tuberculosis is an acute infectious disease. Therefore, until tuberculosis sanatoria are run with some sort of isolation technic, it is somewhat risky to send the acute exudative case into a tuberculosis center. It has been our plan to isolate these cases and keep them at rest till all evidence of their disease has disappeared, after which time their normal routine may be resumed.

The following cases illustrate this type of pathology:

CASE I. A female, 19 years of age, was admitted to our Clinic with the following history: The past month the patient noted an upper respiratory infection with a slight cough. Two weeks later she went to bed because of a sudden rise in temperature. She has been hoarse since. She raised a dram of blood

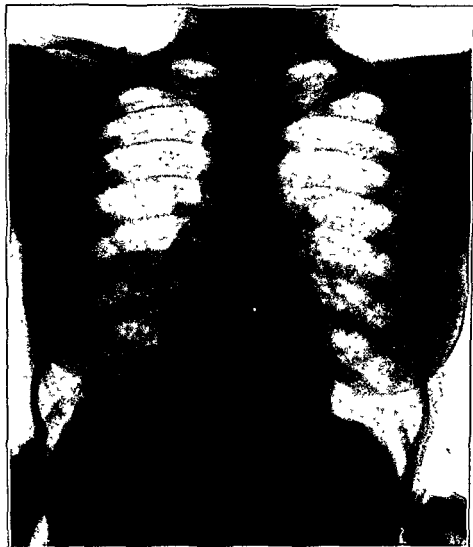


Fig. 20.—X-ray of the lungs of Case No. 1 shows considerable resolution of the exudative tuberculosis in the lower half of the right lung. Six and a half months have elapsed since the onset of the disease.

prior to her examination; then her sputum was blood-streaked for seven days. She coughs and expectorates at the present time. When she first went to bed, her temperature was 101° F. It subsided slowly, and after a week came down to 98° F. Her local physician had examined her and told her that she had a lobar pneumonia. There was a history of a tuberculous contact. Her sister-in-law who lived in the same house had an open case of tuberculosis.

Physical examination revealed the following: Bronchovesicular breathing was heard over the right upper lobe from the apex down to the 2nd rib anteriorly and to the 3rd rib posteriorly. No moist râles were heard over the upper lobe. Bronchovesicular breathing was heard from the 6th rib posteriorly down to about the ninth; moist râles were present in this area. Examination of her sputum demonstrated tubercle bacilli.

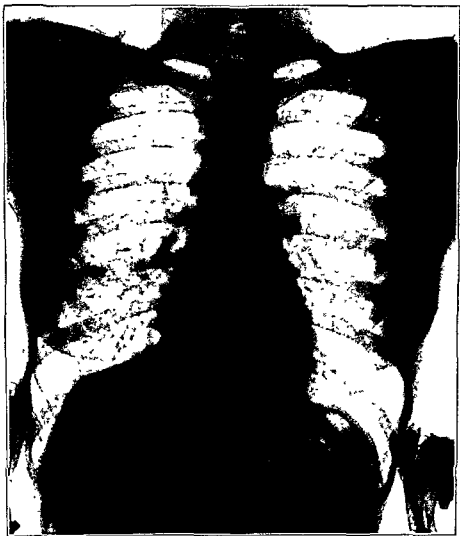


Fig. 21.—X-ray of Case No. 1 about nine months after the onset of the tuberculosis. Resolution has been almost completed

Her x-ray revealed the following: There was an exudative lesion which appeared to be in the process of resolution in the lower half of the right lung. Close to the root area there was an annular shadow about the size of a half-dollar. The process extended from the 4th rib down to the base anteriorly, and from the 6th rib posteriorly down to the base. The extent of the lesion with an annular shadow classified her disease as far-advanced. The patient was put to bed. Her



symptoms rapidly disappeared. Her sputum a few weeks later was again positive for tubercle bacilli. Following that, the patient did not expectorate, and no search was therefore made for bacilli as there was no sputum. The physical signs slowly disappeared and there was a progressive resolution of the tuberculous process. Fig. 18 is an x-ray at the beginning of her disease. Fig. 19 is an

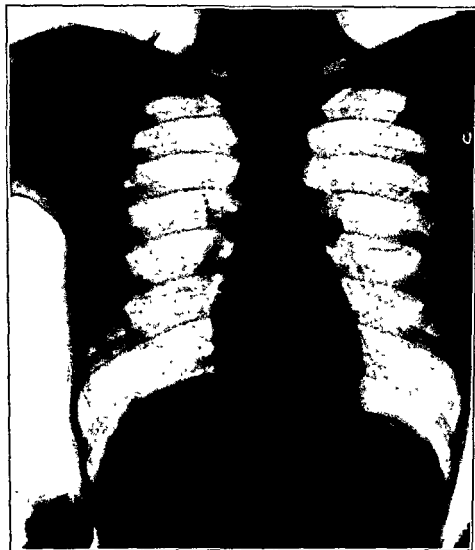


Fig. 22.—An x-ray of the thorax of Case No. 1 taken sixteen months after the onset of the disease. The tuberculosis has disappeared except for a few fibrotic strands in the right lower lobe.

toms, and the x-ray showed considerable resolution. Fig. 21 is taken 8 months x-ray 43 days later. Fig. 20 is an x-ray taken six and a half months after the x-ray in Fig. 18. At this time the patient complained of no cough, had no symp- and 17 days after Fig. 18 in which there is almost complete resolution of the process. Fig. 22 is an x-ray of the patient seven months later. One would now hesitate to make a diagnosis of pulmonary tuberculosis. This patient had been

removed from her tuberculous contact, and is an excellent example of resolution of an extensive tuberculous disease. The treatment of this benign exudative tuberculosis is one of rest. When symptoms disappear, the patient is put on partial rest treatment, being allowed to partake of some exercise. One important factor in the therapy is to isolate the patient from any tuberculous contacts.

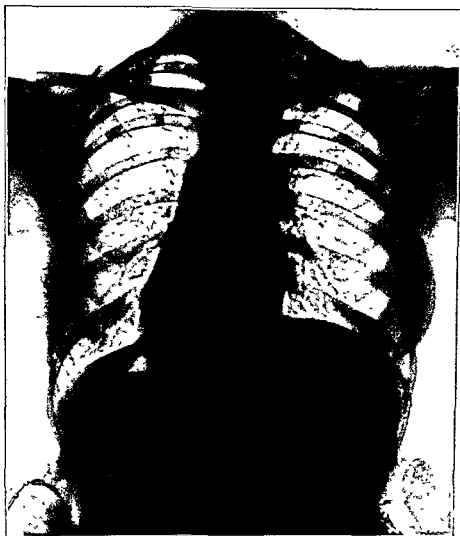


Fig. 23.—An x-ray of a young female (Case No 2) with an exudative tuberculosis in the apex of the right upper lobe. The annular shadow is very suggestive of cavity formation.

The family and close acquaintances must be carefully combed for pulmonary tuberculosis. It is not advisable to send the benign exudative tuberculosis case to the tuberculosis center unless one is sure of absolute isolation from the open case.

CASE II—A female, white, 28 years of age, with a history of contact, came to the Clinic. Her history was as follows: She had been well up through the winter of 1931; a few weeks before admission which was on March 5, 1932, she

complained of a persistent cough with slight expectoration. She fatigued easily. Due to the fact that she had a sister who had had pulmonary tuberculosis she was considerably alarmed about herself. She did not believe that she had lost any weight. She came in chiefly for a check-up because she wanted to be sure that she did not have tuberculosis.

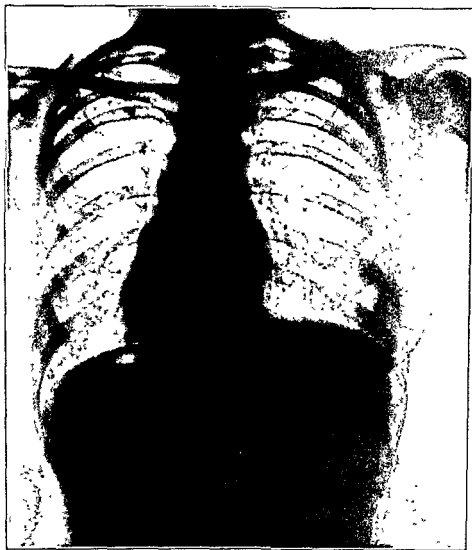


Fig. 24.—An x-ray of Case No. 2 taken 41 days later in which there is a rapid disappearance of the shadows present in Fig. 23.

Physical examination revealed the following: The percussion note was dull over the right upper lobe posteriorly from the apex to the 5th rib. A few moist râles were heard from the apex down to the 6th vertebral spine.

X-ray examination revealed the following (Fig. 23): In the right upper lobe there was a parenchymatous infiltration that extended from the apex down a little below the upper border of the 1st rib. The shadow was not homogeneous. There was a high light in it suggesting an annular shadow that appeared very

much like a cavity. In examining the sputum tubercle bacilli were demonstrable. The patient was put to bed. Her cough rapidly subsided. She lost her expectoration; her appetite improved considerably, and she gained in weight. Forty-one days later her x-ray (Fig. 24) shows a disappearance of the shadows noted previously. The annular shadow suggesting the cavity along with the rest of

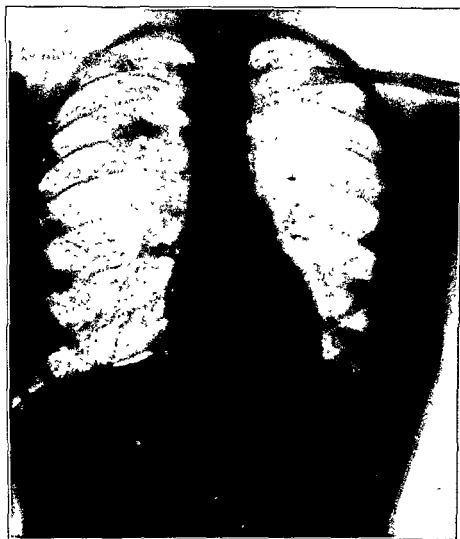


Fig 25—A young female with an exudative tuberculosis in the right upper lobe (Case No. 3)

the shadow that had extended from the apex down to below the upper border of the 1st rib completely disappeared.

The treatment was complete rest in bed until all symptoms disappeared. Following this, with the rapid disappearance of physical signs the patient was put on a modified rest cure. Within two months she insisted on returning to her occupation where she has been since, enjoying good health, having no cough or expectoration. She was separated from her tuberculous contact at home.

CASE III.—A female, 17 years of age, white, with a history of direct contact with an open case of tuberculosis, became acutely ill. She gave the following history: She had been sick for a week complaining of a severe cough and expectoration. Her temperature was as high as 102° F. at the onset but rapidly

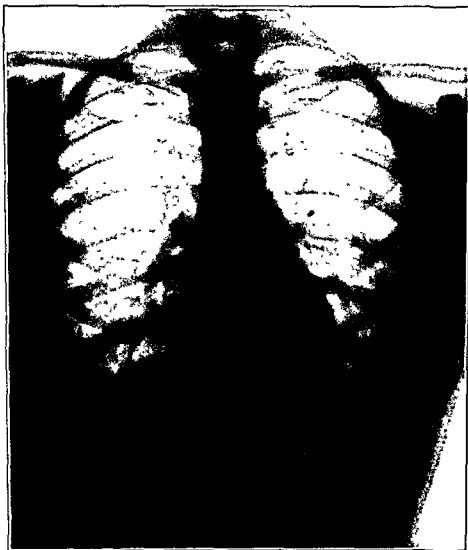


Fig. 26.—An x-ray of Case No. 3 demonstrating the rapid resolution which may take place in benign exudative tuberculosis. Forty-nine days have elapsed since the x-ray demonstrated in Fig. 25.

subsided. She had blood-streaked sputum on several occasions during the first week of her illness.

Physical examination revealed the following: In the right lung dullness was elicited from the apex to the 3rd vertebral spine. Moist râles were heard over this area. Bronchovesicular breathing from the apex to the 4th rib anteriorly. In the left lung there was no modification of the breath sounds or adventitious sounds heard.

Her x-ray of Dec. 17, 1932, revealed the following (Fig. 25): There is an exudative reaction in the right upper lobe which extends from the lower border of the 1st rib down to the 2nd interspace. Its base is towards the axilla and the apex of it lies near the root area. The left lung is apparently normal. Search was made for tubercle bacilli but no bacilli were demonstrable in the sputum. The patient was put to bed; all her symptoms rapidly disappeared. The physical finding disappeared quickly. She was kept in bed for six weeks and again x-rayed. Fig. 26 is an x-ray taken forty-nine days later. This roentgenogram shows a complete resolution of the process. The patient was separated from her tuberculous contact and has been well ever since.

### EXUDATIVE-PRODUCTIVE TUBERCULOSIS.

Exudative-productive tuberculosis has been so designated because of a combined exudative and cellular tissue reaction. The process begins acutely, probably more commonly than benign exudative tuberculosis. The frequency of exudative-productive tuberculosis may be ascribed to the ease of recognition due to the large areas of lung tissue involved and the more frequent appearance of bacilli in the sputum.

**Etiology and Pathology.**—The pathological changes again depend chiefly on the sensitivity of the tissue to tuberculous antigen. Here the infecting dose is larger than in benign exudative tuberculosis. Because of this greater dosage the reaction is more severe. Fortunately there is relatively little lung destruction so that resolution may occur without gross visualization of the previous disease in the lung parenchyma.

This exudative reaction has been frequently termed gelatinous tuberculous pneumonia (Fraenkel and Graff<sup>22</sup>). Besides the serous exudate there is a great deal more fibrin present and the alveoli are packed by polymorphonuclear, round, and with a sprinkling of epithelioid cells. Productive changes (the usual tubercle formation) may occur here and there but most often along the margin of the reaction. Here and there may be seen small areas of caseation.

Due to the fact that there is only a small amount of lung destruction, resolution takes place with almost complete absorption of the whole affair. Inasmuch as the resolution is not uniform throughout the process there may be seen in the roentgenogram irregular areas of aëration which simulate cavity formation. Finally even the walls of these annular shadows are absorbed but in so irregular a manner as to give a moth-eaten appearance to the previously round or elliptical wall of the questionable cavity.

Because of the increase in fibrin and cellular elements resolution occurs more slowly than in the acute benign process. From six months to two years are required for the maximum disappearance of the pathology. Following the absorption of the exudative process a few small scars may remain in the areas where there had been caseation and subsequent excavation. Healing of these areas is by fibrosis and can be noted in the roentgenogram as fibrotic strands. At the periphery there are frequently acinous productive changes from which the disease may progress as a chronic productive tuberculosis.

Though the extent of the disease is usually in the moderate or far-advanced stage, occasionally it may occur as a minimal lesion.

**Clinical Picture.**—The disease begins as an acute process and can easily be mistaken for a lobar pneumonia. The symptoms at first are almost identical. Fortunately, again, hemoptysis appears frequently enough to help in the differential diagnosis. The temperature in this type of tuberculosis may persist from two to three weeks and usually subsides by lysis. Cough and expectoration rapidly appear, the expectorating being more copious than in lobar pneumonia. Search for tubercle bacilli at this period often clinches the diagnosis. The persistence of physical signs and the delay in resolution are also important leads to the recognition of this acute form of tuberculosis.

When small areas of lung are involved the symptoms are not very striking so that the disease is often diagnosed as a mere grippal affair. With the subsidence of temperature the affair may pass completely unrecognized. This can be observed in tuberculosis hospitals where sudden rises in temperature and pulse rate which persist for a few days are investigated. In our institutions these patients are immediately x-rayed. New areas of exudative reaction are frequently noted in the roentgenogram. This practice is not universal in our tuberculosis institutions. The diagnosis of gripe is attributed to these common allergic spreads.

Following the acute stage, cough and expectoration may persist for a few weeks and then subside. The patients rapidly add weight and if it were not for the persistence of physical signs and pulmonary x-ray shadows, they would be discharged as cured. The prognosis in these cases is very good.

**Sputum.**—In the early stages of this infection tubercle bacilli are easily demonstrated in the stained smears of the sputum. We wish to emphasize the importance of the search for bacilli early in the disease because with the disappearance of expectoration the possibility of demonstrating bacilli is lost and the diagnosis of tuberculosis may be questioned. Bacilli are present in low Gaffky counts. Because of this a longer search than the routine one is advised.

**Physical Signs.**—At the beginning, with an extensive lesion, the physical signs are many. There is altered breathing, usually bronchovesicular in character with coarse moist râles which are quite high in pitch. The percussion note, due to the extensive involvement, is usually dull. There is a frequent occurrence of musical râles, both of the sibilant and the sonorous variety. However, we must constantly keep in mind the fact that when the pathology is central there may be an absence of abnormal findings. The fact that negative physical findings do not rule out pulmonary involvement must be stressed continuously. Because of the extensive lesion that is usually associated with this form of disease, the physical signs are very definite at the onset of the infection. As resolution occurs the signs become less marked and finally disappear.

**X-ray Examination.**—At the beginning of the disease, the roentgenogram usually demonstrates an exudative inflammatory form of reaction which varies in size and location. Inasmuch as the frequent site of the tuberculous infection is in the upper lobe, the lower border of the process usually rests upon the

interlobar fissure between the upper and middle lobes. The interlobar space is sharply outlined. The shadow is that of any pneumonic infiltration, usually of a homogeneous density. The process is very difficult to differentiate from any other acute form of exudative tuberculosis. With serial x-rays the type of infection is easily determined. The exudative process begins to resolve, leaving a peculiar acinous mottling throughout, so that in the mid-stage of this disease the picture may resemble an acinous productive tuberculous process. The absorption is not uniform so that one may see very irregular shadows that suggest cavity formation. However, continuous serial x-rays demonstrate further resolution with disappearance of all annular shadows. It is not uncommon to see what appears to be the wall of a large cavity begin to break up in sections much like the bursting of a rocket with a final complete disappearance of what was previously supposed to be a cavity.

The prognosis should not be made on the first x-ray but on the serial pictures and also on the associated clinical picture. In other words, an extensive x-ray lesion in a patient without symptoms suggests the probability of exudative productive tuberculosis. Another important factor in forming this conclusion is the absence of tubercle bacilli or, at most, their presence in low Gaffky counts. In the caseous-pneumonic process with cavity formation the Gaffky count is usually high. In the description of the course of the disease we brought attention to the rather toxic acute stage with a rapid fall in the temperature and pulse rate. The symptoms are rapidly lost, so that at the end of six weeks to two months, the patient is afebrile, has a normal pulse rate, and very few complaints. Cough and expectoration may have completely subsided. The x-ray changes, however, are very much slower. Resolution takes a long period of time, from six to twenty-four months. A great many of the patients return to their occupations long before resolution has been completed. After a period of from twelve to sixteen months, it is difficult to recognize the process, even by roentgen-ray.

**Prognosis.**—From what has been previously mentioned, this form of tuberculosis runs a benign course. The process usually slowly resolves, leaving some evidence of fibrotic strands and acinous productive changes in the x-ray. Occasionally the acinous productive lesion continues on, and the prognosis then is the same as that established in the chronic productive forms of tuberculosis.

**Treatment.**—The treatment of this type of tuberculosis can be divided into two stages—the acute, and the chronic one. The treatment in the acute stage is entirely symptomatic. The patient is kept in bed as long as there are toxic symptoms. With bed rest, symptoms are soon lost. Cough and expectoration quickly disappear. Weight is rapidly put on. After a few months the patient feels well. The difficulty then is to continue the rest therapy. It has been our policy to keep the patient with the exudative-productive type of tuberculosis on a modified rest treatment until there is complete resolution of the disease. There is a marked temptation in the early stages of an acute exudative-productive tuberculosis to use collapse therapy. Our experience has been that in the acute stage of any exudative tuberculous process there can be little compression. Should the caseous-pneumonic lung be compressed, there is a constant impending complication of a spontaneous pneumothorax. It is therefore advisable, in all acute forms



of tuberculosis to wait for six to eight weeks. By that time there should be no difficulty in establishing which of the three exudative types one is dealing with. We do not advise collapse therapy once the diagnosis of an exudative-productive process is established. If pneumothorax is induced, the treatment would be continued for from three to five years. Why carry out so long a mode of "therapy"

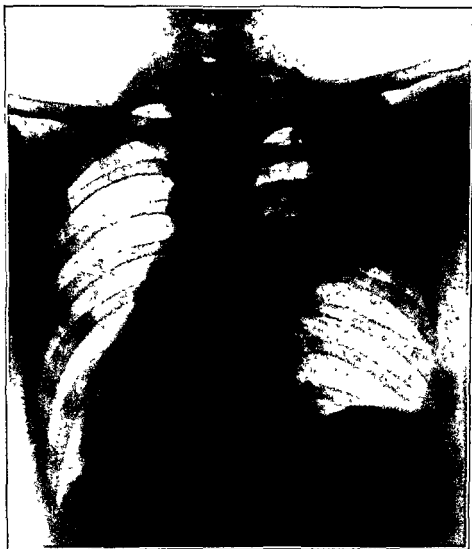


Fig. 27.—Fig. 27 is an x-ray of an exudative productive form of pulmonary tuberculosis (Case No. 1, page 71) Figs. 28, 29, 30, 31 and 32 demonstrate the slow and irregular mode of resolution of this type of tuberculosis.

in an individual whose process will completely and spontaneously resolve in eighteen to twenty-four months?

*Benign Course.*—Most workers in tuberculosis sanatoria have had the experience of seeing complete resolution occur in cases where a bad prognosis had been prophesied because pneumothorax could not be induced. After a period of six months one is surprised to find hardly any trace of the tuberculous disease. Had

pneumothorax been induced, it would have unjustifiably been given the credit for the rapid resolution. The reasons against the use of pneumothorax in exudative-productive tuberculosis hold good also against the use of any other surgical procedure. It is our impression that a great many of the phenomenal recoveries that occur with phrenicectomy can be ascribed to the benign course of the exudative-

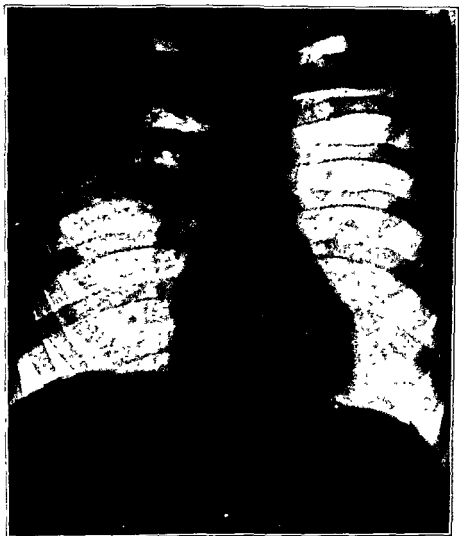


Fig. 28—There has been considerable resorption in the lapse of one month. Note the disappearance of the small annular shadow present in Fig. 27 between the fourth and fifth posterior ribs.

productive type of tuberculosis. Phrenicectomy is frequently performed when pneumothorax cannot be induced. In a few weeks definite evidence of resolution is observed. How can one help but assume then that phrenicectomy as a single operation is of value in tuberculosis? It is only after long experience with the exudative types of tuberculosis that one begins to realize that the benign exudative and the exudative-productive tuberculous processes do resolve spontaneously.

The same can be said concerning the use of any drugs in the treatment of pulmonary tuberculosis. When there is noted the marked differences of opinion in the treatment of pulmonary tuberculosis, one can readily understand that there are types of tuberculosis that clear up spontaneously.

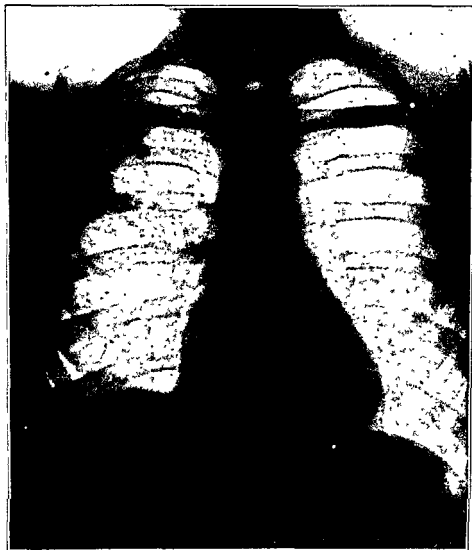


Fig. 29.—Further resolution has occurred. The irregular absorption produced an elliptical shadow suggesting a large cavity.

In the evaluation of any form of treatment one must be familiar with the various types of pulmonary tuberculosis. Any treatment in the acute benign or in the acute exudative-productive form of tuberculosis will produce good results. Again we must emphasize the importance of elimination of contacts.

The family should be carefully searched for open cases. One must not depend wholly upon physical examination in the check-up of contacts. It is not advisable to send these hypersensitive individuals to the tuberculosis center unless we are sure that they will be isolated from open cases. Patients with exudative-pro-

ductive tuberculosis are hard to manage in the chronic stage. They feel so well and have so few symptoms that they usually insist on returning to their normal routine of life. It has been amazing to find how resolution occurs in a large percentage of these cases in spite of the fact that they return to their normal routine. The following case will illustrate this type of tuberculosis:



*Fig. 30—An x-ray taken 4 months after the x-ray in Fig. 29. In spite of marked clinical improvement there has been no further evidence of resolution. Cough, expectoration and all symptoms have disappeared. The patient has put on a great deal of weight. The elliptical shadow suggesting a large cavity persists.*

CASE I.—A white male, 25 years of age, reported to our Clinic on November 29, 1929. He had no complaints. He had been to Saranac Lake since July 1, 1929 and came to the city that he might clear up his business affairs. He had no cough or expectoration. He had gained forty pounds in weight in five months. He gave the following previous history:

In June, 1929, he had a pneumonic condition and examination of his sputum revealed many tubercle bacilli. An x-ray taken of his lungs (Fig. 27) revealed an acute exudative reaction which involved most of the upper lobe and some parts of the left lung. As soon as his temperature subsided he was sent to Saranac Lake, N. Y. Within a month there was an improvement in his condition.

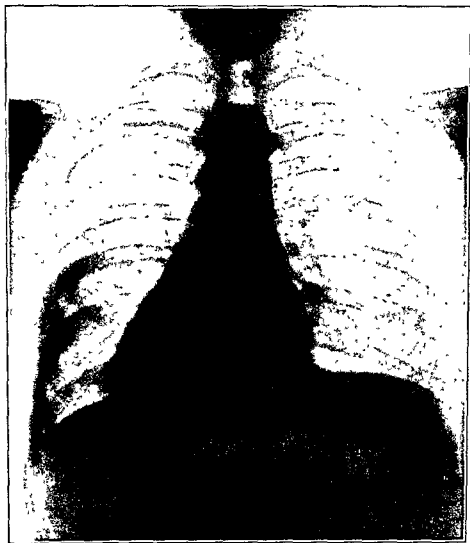


Fig. 31.—More than 12 months have elapsed. The patient has returned to his occupation. He has had no return of symptoms. Note the breaking up of the outline of the elliptical shadow which had suggested a large cavity.

His x-ray (Fig. 28) also showed the beginning of resolution. The next month he lost all his symptoms and began to gain weight rapidly. In his first x-rays (Fig. 27) there was a highlight in the second interspace which suggested a small cavity. Another x-ray, taken forty-eight days later, disclosed an irregular resolution with a large elliptical shadow in the upper lobe. The small annular shadow had in the meantime disappeared (Fig. 29). After an examination in November,

1929, the patient was told he had scant physical findings but still had considerable x-ray pathology. He was advised to remain at Saranac Lake. He disregarded the advice and came down to the city.

Physical examination revealed no abnormal findings. The x-ray examination was disconcerting. There was some pathology in the right upper lobe with a

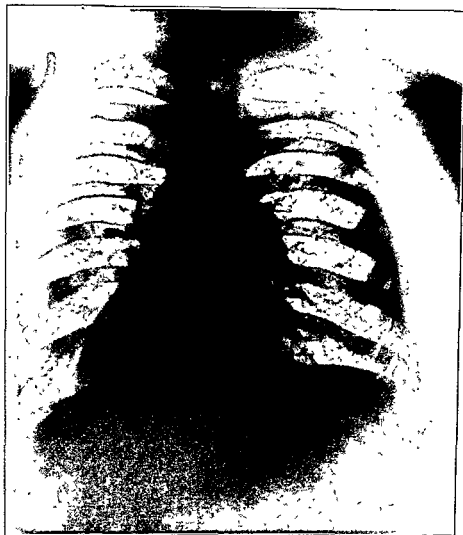


Fig 32—Fourteen months later. The patient has had no return of symptoms. Note almost a complete clearing of the parenchymal shadows in the right upper lobe. There are a few small productive areas present in the right upper lobe.

large elliptical shadow between the first and second ribs anteriorly. This shadow resembled a large cavity (Fig. 30).

The general condition of the patient with no cough or expectoration suggested the probability of the exudative-productive type of tuberculosis. We decided to allow him to return to his occupation provided we had the opportunity to frequently check up his condition.

The patient has remained well. He has been actively engaged in business. The process slowly resolved (Fig. 31). An x-ray 20 months after the onset of the disease demonstrates the breaking up of the elliptical ring shadow. There has been a complete resolution of the disease (Fig. 32).

### CASEOUS-PNEUMONIC TUBERCULOSIS.

Caseous-pneumonic tuberculosis is one of the most frequent types of pulmonary tuberculosis. In the past considerable confusion has arisen because of the failure on the part of the clinician to recognize the various acute and chronic phases of this single clinical entity. The acute stage has been called tuberculous pneumonia, with little attempt to differentiate this malignant form of infection from the acute onsets of the resolving exudative affairs previously discussed. Following soon after the acute onset caseation and softening take place. When the caseous material is sloughed out and the necrotic mass disposed of, the chronic phase of the disease is reached. Here nature starts her healing process with the deposition of considerable fibrotic tissue. Because of this, the term fibroid phthisis has been given to the disease. Failure to recognize this chronic stage as the end-result of a previously acute stage of tuberculosis has given rise to the loose use of misleading terms such as fibro-ulcerative and fibro-caseous tuberculosis as though each term were describing a different type of disease. All are part of the same genetic affair, a form of tuberculosis which is so common that the old teaching of the rarity of acute tuberculous pneumonia must be abandoned as untrue.

**Pathology.**—In this type of disease, probably because of the massive dose of tubercle bacilli, there has been a tremendous stimulation of the body cells. The cell stimulation, however, has been excessive, and as a result there is over-irritation and the cell destruction. The whole area undergoes caseation. This area may vary in size from that of the acinus, the unit of lung structure, to the entire lobe, or even lung. The alveoli contain an albuminous exudate, much fibrin and cellular elements. When caseation occurs, the alveolar network loses its identity, the elastic fibers being one of the last structures to disappear. As a result the whole area becomes a more or less homogeneous mass. As might be expected, a patient with this type of disease is sick and toxic. Inasmuch as all this caseous material must be sloughed out before healing can occur, cough is severe and expectoration profuse. When finally the necrotic slough has been disposed of, there remains an empty cavity in place of the caseous tissue which has been expectorated. It is now that repair begins to predominate. Productive scar tissue surrounds the area. Contracture of the scar occurs, with the subsequent distortion of the mediastinum or thoracic contents. It is this phase, the chronic end-stage of the above acute caseous-pneumonic tuberculosis that accounts for such a large proportion of our clinic attendance.

**Clinical Picture.**—Though the onset is acute, the clinical course suggests a chronic disease. There are intermittent periods of activity and quiescence. These alternating periods of well-being and toxemia in this form of tuberculosis depend upon the frequency of superinfection. To understand this phase of pulmonary

tuberculosis one must be familiar with the abrupt onset of the exudative infection and the resultant caseation and cavity formation from which there is a constant shedding of tubercle bacilli to cause further superinfection. The clinical picture may be further clouded by infection in either the intestinal tract or the larynx. When these complications occur there is occasional difficulty in determining whether the toxemia is due to the process in the lung or to the complications.

**Acute Phase.**—In the acute phase the onset is sudden and the toxemia is severe. At the beginning there may be but little complaint of cough and expectoration. The picture resembles an acute respiratory infection, simulating either a lobar or a bronchiopneumonia. Cough, however, soon becomes distressing. The expectoration of phlegm, scant at first, becomes profuse and laden with tubercle bacilli. Hemoptysis is frequent at this period. The plateau-like curve of the temperature suggests a pneumonic condition and may remain high for many weeks. More often, after the first two weeks the peak becomes lower, fluctuates, and resembles a septic temperature. Low or subnormal in the morning, the temperature may reach 103° to 104° F. in the late afternoon. When the necrotic mass is finally sloughed away and expectorated, the temperature tends to reach the normal level. The pulse in the acute phase follows the temperature curve. The pulse rate may be as high as 120 and rarely comes back to the normal, even long after the caseous tissues have sloughed out. The picture of toxemia persists until caseation and sloughing have been completed. The toxemia is directly proportional to the amount of necrotic tissue that remains to be sloughed out. Finally when the whole necrotic mass is expectorated, the symptoms of toxemia disappear provided there has been no further superinfection.

**Chronic Phase.**—With the disappearance of symptoms of toxemia and a return of a low or normal temperature, the patients perk up and become interested in life again. The appetite improves and weight may be rapidly added. The only complaints are cough and expectoration. The marked change in the clinical picture gives courage and hope to both the patient and the doctor. As has been previously stated, the chief complaint concerns both cough and expectoration. The cough persists. The expectoration is more or less profuse with tubercle bacilli easily demonstrable. Like the sword of Damocles, this cough and expectoration with positive sputum hang as a constant threat over the head of the patient. And rightfully so, for with the positive sputum the chances of bronchogenic spread are great. As long as no new infection occurs, the patient is "temporarily safe." No one who has dealt with tuberculosis has failed to experience the bitter disappointment upon viewing the x-ray of a patient who has passed through the acute toxic stage and is now seemingly well. Although the temperature and pulse rate are close to the normal range and the physical findings scant, the x-rays may now disclose single or multiple cavities in the area where there had previously been the exudative lesion. The sputum, too, is positive. And why is disappointment so keen? Simply because experience has shown that patients with cavity formation are usually doomed to die. The statistical reports of many workers have shown that this conclusion is correct, Barnes and Barnes,<sup>53</sup> for example, stating that 95 per cent. of such patients are dead within five years. It is in this condition that the patient enters the chronic



stage of the disease, free of most symptoms of toxemia but with cavity formation following the expectoration of the necrotic and caseous tissue. Cough and expectoration usually persist. From now on the recurrence of symptoms indicates new areas of infection in the same or the opposite lung. When this new area of

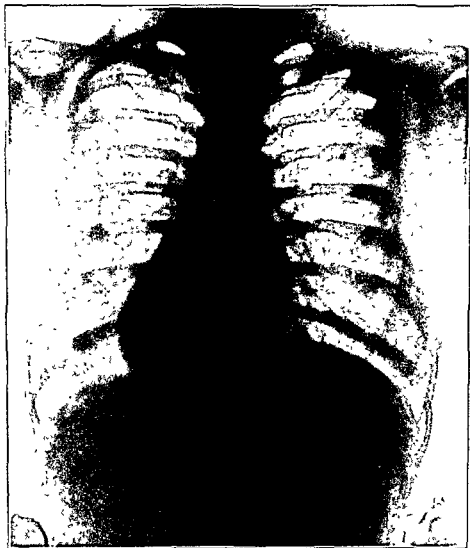


Fig. 33.—A young white woman with small cavity in the left upper lobe. The patient was discovered accidentally in a contact study. Signs and symptoms scant. Patient insisted on continuing with occupation. Advised to go to sanatorium for collapse therapy. Diagnosed as minimal caseous-pneumonic tuberculosis with cavity formation. The small cavity is in the left upper lobe. It is almost hidden in the anterior portion of the first rib. Prognosis questionable.

involvement resolves or excavates, the disease again becomes quiescent. One can now understand the varied clinical picture of the chronic phase of caseous-pneumonic tuberculosis.

Complications of both *laryngeal* and *intestinal* tuberculosis are common, the intestinal infection being exceedingly frequent. The toxemia associated with

tuberculosis of the intestines frequently confuses the clinical pulmonary picture. The patient who has had no pulmonary x-ray changes in months may become actively ill. With no evidence of new disease in the lungs the intestinal tract is to be regarded suspiciously as the cause of the toxemia. When the larynx becomes involved, there are sufficient symptoms to direct attention to the larynx.

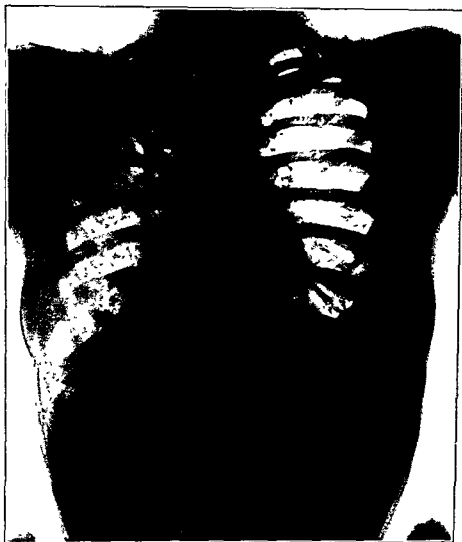


Fig. 34.—After consenting to go to a sanatorium the patient changed her mind because she felt so well. Fluoroscopy one month before this film showed the same appearance as Fig. 33. Four days before the present film pain was noted in left thorax. Temperature 104° F. Cough and expectoration. Physical examination and x-ray demonstrate an acute and extensive spread of the disease in the left lung.

The clinical picture is not always as dramatic as the above description. When small areas of the lung are involved, the symptoms may resemble a grippal affair. The small caseous area is quickly sloughed away. The patient is again normal. Physical findings are absent or scant. Nevertheless this patient goes into the chronic stage of the disease with almost the same risks as the moderately or

far-advanced case. Superinfection is probable even with a small cavity. The following cases demonstrate the above situation.

**CASE I.**—A young woman of 18 years, white, working in the fur trade came to the Clinic at our request because of contact with an open case of tuberculosis. She had no complaints except for a slight cough. She had no expectoration. She complained of a grippal affair two months previously which quickly subsided. She had consulted no physician. Her temperature was 98.6 at 6 p. m. The pulse rate after a day's work was 90. Physical examination was normal except for some dullness on percussion over the left upper lobe. Fluoroscopy and x-ray examination revealed a small cavity in the left upper lobe. The cavity was elliptical in shape, the lower portion almost funnel-shaped. The size of the cavity was two by two and a half centimeters in its largest diameter. The cavity was situated in the center of the upper lobe about opposite the first rib anteriorly, and between the third and fourth ribs posteriorly (Fig. 33). The accentuation of the draining bronchus gave the cavity a tennis-racket appearance.

A diagnosis of chronic caseous-pneumonic tuberculosis with cavity formation was made. A questionable prognosis was given and the patient was urged to go to a sanatorium for collapse therapy. At first the patient refused. She stated that she was in good health and insisted on continuing her occupation. She did consent to come in every fortnight for a check-up. Three weeks after her initial visit she was examined again. The cavity appeared smaller. In spite of her good clinical condition she was urged to go to a sanatorium for collapse therapy of the left lung by pneumothorax. She consented. Her friends persuaded her not to go and we lost track of her. She came back four weeks later and told the following story. She felt well until four days ago when she had pain in her left thorax. Her temperature reached 104° F. that night. She stayed in bed for four days. She became alarmed because of the persistence of the temperature and the appearance of a distressing cough with expectoration.

The patient was acutely ill. Her temperature in the morning was 101° F. She had signs of an infiltration of the upper two-thirds of the left lung. Fig. 34 shows the acute and extensive spread of the disease in less than 30 days. One now understands what is meant when the statement is made that a patient in the chronic stage of caseous-pneumonic tuberculosis with cavity formation and no signs of activity is only "temporarily safe."

### PHYSICAL DIAGNOSIS.

The many changes in tissue structure in caseous-pneumonic tuberculosis continually alter the physical findings. At the onset the findings are similar to any acute pneumonic process. A flat or a very dull note is heard on percussion and pure or modified bronchial breathing may be heard. As soon as softening occurs moist râles appear. The exudative inflammation may be centrally located and then, of course, the findings may be scant and sometimes even absent.

As the process sloughs out, more and more of the bronchial element is lost and replaced by cavernous breathing. Pure cavernous breathing is rarely heard. In the process of evacuation of the slough the caseous area becomes quite honey-

combed with small cavities. In this stage the râles sound more moist, higher in pitch and have peculiar bubbling and bursting qualities.

With cavity formation the physical findings begin to change. They depend a great deal on what happens to the outlet of the cavity and the lumen of the

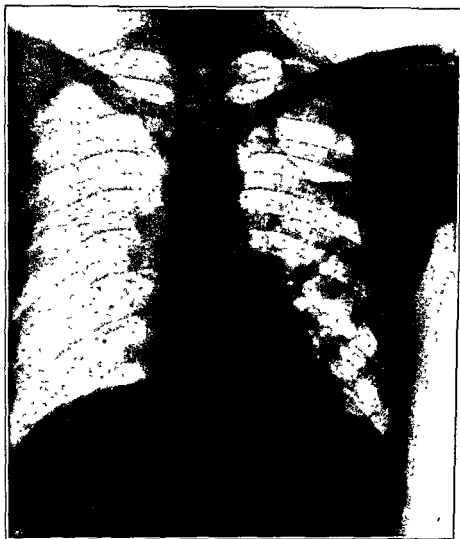


Fig. 35.—Note the large cavity in the left upper lobe. There is no displacement of the mediastinum. The left intercostal spaces are even wider than on the right side. The lung tissue overlying the cavity is emphysematous and masks the physical findings of the underlying disease.

draining bronchi. A small or large opening into the cavity alters the character of the breath sound. Cavernous sound is heard with the large opening, and the musical rhythmic high-pitched amphoric sound is heard with the small opening.

*Silent Cavities.*—The intensity of the breath sound depends a great deal on the patency of the draining bronchi. When the latter are obstructed, the intensity may be so faint as to allow no recognition of the character of the sound. In

the centrally located cavity there is an associated compensatory emphysema of the surrounding lung tissue. The intensified normal vesicular sounds may completely mask the underlying pathology. Many of us have been surprised because of the absence of physical signs suggesting cavity and the presence of an x-ray shadow of one (Fig. 35). It has been our experience that a large number of

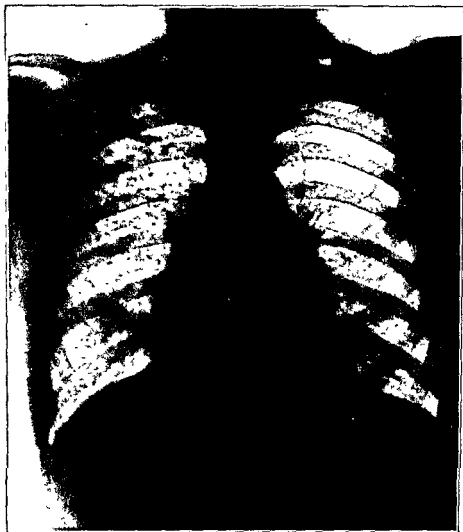


Fig. 36—In the right upper lobe there is a good-sized cavity. From this source there is a bronchogenic seeding through the whole right lung.

cavities are silent. Fortunately, in most instances some altered breathing, usually bronchovesicular in character, and moist râles are present.

From the patent cavity there is frequently a seeding down through the lung and because of the diffuse acinous infiltration many moist râles may be heard over the whole lung (Fig. 36).

In the process of healing, the involved portion of the lung may become small, dense and contracted. Whether or not this is due to atelectasis is beyond

the scope of this discussion. It would seem that occasionally atelectasis is the mechanism involved in the shrinkage of the lung. When a condition of this sort arises, serious disturbances in the normal structural relationships within the thorax take place. Solid airless lung is a fairly good sound transmitter so that if



Fig 37.—A retraction of the whole right upper lobe with distortion of the mediastinum and trachea. There has been a marked narrowing of the intercostal spaces. This solid lung, though airless, becomes a good transmitting medium and the noises in the trachea and bronchi are brought to the surface of the overlying thorax.

it is the only lung tissue interposed between the examiner's ear and the large tubes, there will be a direct transmission of bronchial or tracheal breathing. On the other hand, if a compensatory emphysema occurs so that the contracted lung is enveloped by emphysematous lung tissue, no such sound will be heard. Râles are of frequent occurrence, however, probably due to the distortion of the bronchial tubes and a resultant stagnation of secretion. With such marked dis-

turbances in structure, there can frequently be seen associated shifting of the mediastinum as evidenced by deviation of the trachea or shifting of the heart and the mediastinum. Changes in the percussion note may be similarly influenced by the distortion (Fig. 37).

*Resumé.*—In the preceding paragraphs we have attempted to describe the differences in the physical findings with the many changes occurring in the pathology of this type of tuberculosis. We wish to emphasize that in the minimal lesions the physical findings are scant or absent. Even in caseous-pneumonic tuberculosis the absence of physical findings does not rule out the disease.

### X-RAY EXAMINATION.

Many and rapid x-ray changes may be seen in caseous-pneumonic tuberculosis. At the onset a dense exudative shadow is cast in the x-ray film. By means of serial pictures can be followed the softening and excavation with the formation of multiple or single cavities. Coincidental with softening there are many opportunities for bronchogenic spread, which accounts for both rapid and numerous changes in the serial x-rays. It is the exception rather than the rule for no changes to occur in the presence of cavity formation. With a cavity in an upper lobe there may be an acinous seeding down through the whole lung (Fig. 36). On the other hand a spill of the contents of the cavity into the adjacent lung tissue may produce a rapid extensive exudative lesion throughout a whole lobe or lung (Figs. 33 and 34). The character of the reaction depends primarily upon the dose of the tuberculous antigen although an important rôle is also played by the hypersensitivity of the tissues to the antigen. We can now understand the variegated picture that may be seen in the x-ray film.

The importance of the x-ray in caseous-pneumonic tuberculosis lies in the demonstration of *cavity formation*. In the presence of cavity the prognosis is always questionable. There are various forms of cavity. Many classifications of cavity have been described. Many investigators believe that the character of the cavity has a decided bearing on the possibility of cure. They believe the thin wall cavity lends itself to collapse treatment whereas the thick walled cavities are difficult to compress. Others believe the size of the cavity is also an important factor. They stress the frequent spontaneous disappearance of the small cavity. We have found from experience that all true cavities, small or large, thick walled or thin walled, are a constant threat to the life of the patient. The x-ray has been of great help in aiding us to form this conclusion.

The x-ray also yields information of the first order with regard to the *position of cavities*. Over cavities close to the periphery of the lung there may be considerable thickening of both the visceral and parietal pleura. Thick bands of adhesion may form or the pleural space may be completely obliterated. Both bands and obliteration of the pleural space have an important influence on the closure of the cavity. In central cavities there is little pleural involvement. These points will be discussed more in detail elsewhere.

In spite of the excellent aid given by the x-ray we are extremely hesitant to attempt any classification of cavities. The shape and appearance will depend a great deal on the condition of the bronchus leading to the area of the lung

involved. We believe, however, that a workable classification can be presented, a classification which justifies itself by its ability to explain certain observations as we see them clinically, and which is of aid in discussions of therapy. Both the x-ray and the clinical picture as well as the postmortem examination have helped to identify the different types.



Fig 38.—An x-ray demonstrating early and late phases in cavity formation. In the left lung there are multiple irregular ragged small cavities which have a moth-eaten appearance. In the right upper lobe there is a large cavity of the progressive type. Almost the whole upper lobe has been sloughed out.

We have attempted to divide the different forms of cavity formation into six types. The *first* form is the *early cavity formation* following softening and sloughing out of the caseous material. The walls are thick, irregular and ragged. The cavity may be single or multiple and connected.

The *second* type is a *single cavity* which may be stationary for a short time and then become progressively larger. A wall of tuberculous granulation tissue is formed around the cavity. The tubercles enlarge and caseate and the cavity



slowly and progressively enlarges. Usually it takes on a spherical shape. The cavity may finally involve a lobe or a whole lung. This type of cavity has been called the chronic progressive cavity. The bronchus when patent, presents the following additional factors. The size of the cavity changes on inspiration and expiration, being smaller in the latter phase of breathing. With a wide patent



Fig. 39.—A cavity of the chronic progressive type. The extension of this cavity will be noted in Figs. 40 and 41.

bronchus there may be no narrowing of the interspaces. Figs. 39, 40 and 41 demonstrate the chronic progressive cavity.

The *third* form of cavity depends a great deal on the *condition of the bronchus* leading to the area of lung involved.

Because of tuberculous granulation tissue and thick tenacious secretions there is a check-valve mechanism. Air is slowly injected during inspiration and escapes with great difficulty during expiration. Apparently there is an accumula-

tion of gases in the cavity and it slowly balloons out. Figs. 42, 43, 44 and 45 illustrate the check-valve cavity. This type of cavity may assume an immense size although the original loss of tissue may be relatively insignificant. The shape of the cavity is spherical. It appears to enlarge in a manner similar to the chronic progressive cavity except that the enlargement occurs without any evidence of



Fig. 40—A wall of tuberculous granulation tissue is formed along the wall of the cavity. The tubercles merge and caseate and the cavity slowly and progressively enlarges.

peripheral invasion around the wall of the cavity. These large cavities are silent on physical examination. Furthermore the lung tissue around the whole cavity is normal and the breath sounds may be vicarious in character. The trachea is in the normal position and the interspaces on the diseased side are wide. With a flexible mediastinum the shift is to the normal side on expiration. There is no change in the size of the cavity on inspiration or expiration. Due to the obstruc-

tion there is frequently a retention of secretion with a fluid level in the cavity (Fig. 46). The patients cough and expectorate little. The large bronchus draining this cavity is clearly seen in the x-ray and has a string appearance. When the bronchus is greatly accentuated the cavity and bronchus give a tennis-racket illusion.



Fig. 41.—After 3 years of progression: almost the whole right lung has been excavated (see Figs. 40 and 41).

With a bronchus that is almost completely occluded it is easy to understand how spontaneous closure may rapidly occur. Whenever the bronchus becomes completely obstructed the gaseous contents of the cavity are absorbed. Inasmuch as the walls of the cavity and the surrounding lung are soft and flexible, the cavity becomes smaller and finally disappears. The rapidity of closure of the cavity depends upon the rapidity of the gaseous diffusion. Disappearance may be without a trace but as Tchertkoff<sup>54</sup> of our service has demonstrated again

and again, a linear scar frequently marks the site of the cavity (Figs. 47 and 48). As might be expected, spontaneous closure is very common in this type of cavity.

The *fourth* type of cavity is the *smooth wall cavity* with open bronchus. Apparently the process in the wall of the cavity has stopped progressing and

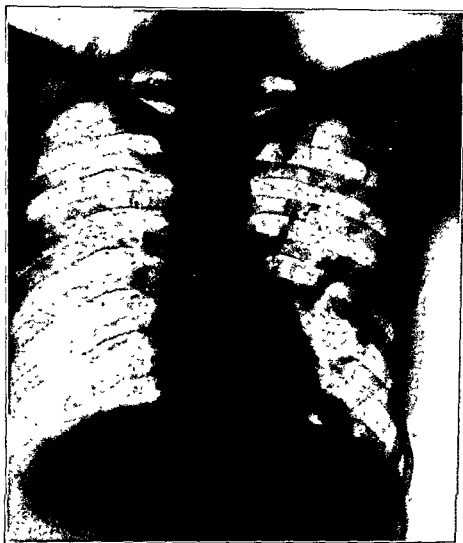


Fig. 42.—An x-ray of a check-valve cavity. Note the spherical appearance of the cavity in the left upper lobe. There is a small amount of fluid at the bottom of the cavity. There has been no displacement of the trachea and mediastinum. There has been no narrowing of the intercostal spaces. The bronchi leading to the cavity are accentuated. See Figs. 43 and 44.

becomes cicatricial. These cavities do not progress. Because of the few bacilli shed from their walls superinfection is infrequent and the prognosis is usually good. The open bronchus with free access of atmospheric pressure gives a circular appearance to this type of cavity. Fig. 49 demonstrates this type of cavity.

The *fifth* type of cavity is the *thick wall cavity* in which there has been a closure of the bronchus. There is little or no gaseous interchange because of the avascular nature of the wall of the cavity. This type of cavity remains unchanged. It resists all forms of compression therapy and remains unchanged except in

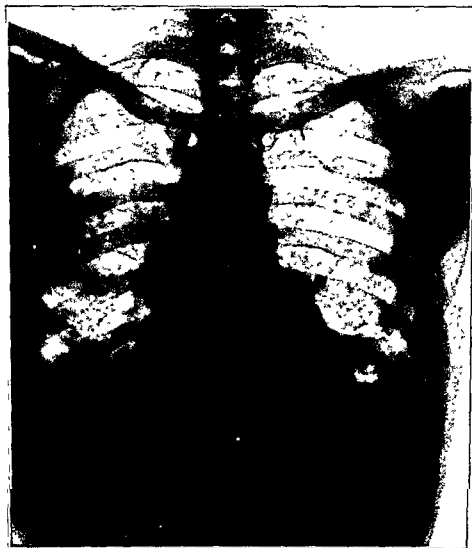


Fig. 43.—The check-valve cavity in Fig. 42 has now increased in size. Six months have elapsed. A phrenic neurectomy had no influence on the progression of this cavity. The breath sounds over the left upper lobe were emphysematous in character and masked all signs of an underlying pathology.

shape with pneumothorax and thoracoplasty. Fig. 50 is an illustration of this type of cavity.

The *sixth* and final type of cavity should be mentioned. This variety is frequently called *bronchiectatic cavity* formation. These cavities are seen in the retracted lung (Fig. 50A) and distinctly identified by bronchography with lipiodol (Fig. 50B). At postmortem they are identified as cavities into which the

bronchi abruptly end. The term is a misnomer and has been used because of the x-ray simulation to saccular bronchiectasis, especially when outlined with lipiodol.

Frequently where there is a check-valve mechanism, the cavities do not enlarge. This may be explained on the basis of an active interchange of gases between the vessels in the cavity wall and the gaseous contents, or to a very

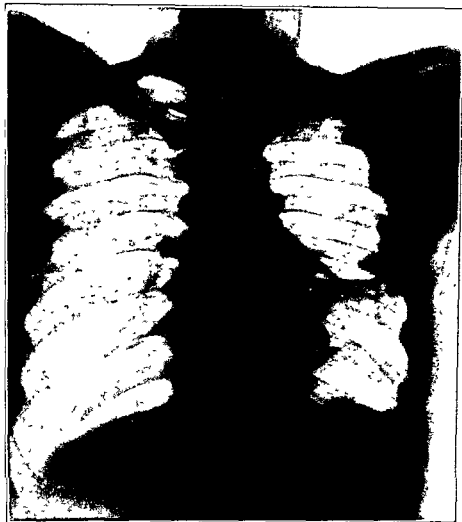


Fig. 44—Note the huge size of this check-valve cavity. Two years and eighteen months have elapsed since the x-ray in Fig. 43. Breath sounds over the left upper lobe are still emphysematous. One would hardly suspect an underlying cavity. The intercostal spaces and mediastinum still maintain their normal position.

small lumen which admits very small quantities of air. These cavities may retain their same size and shape over years. They frequently show an increasing retention of secretions.

Figs. 45 and 46 illustrate the above type. Note the slight fluid level in No. 45 and the increasing fluid content of the cavity in Fig. 46. A spontaneous opening of the bronchus may take place at any time with a severe superinfection

of the surrounding lung tissue. On the other hand these cavities frequently close spontaneously. (Fig. 46A).

*Closure of Cavities.*—The closure of cavities may occur spontaneously. One can never be sure, however, whether the cavity may heal or reopen. Figs. 51, 52 and 53 demonstrate the spontaneous closure and reopening two years later.

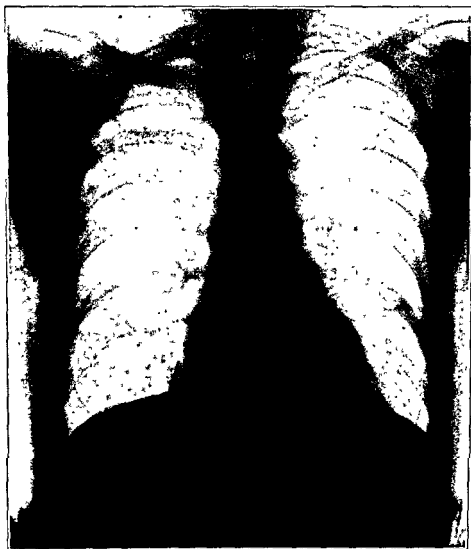


Fig. 45—A check-valve cavity in the right upper lobe with a fluid level. See Fig. 46.

Dr. Coryllos pointed out in his chapter on Pathological Physiology that the closure of the cavity depends upon the absorption of the contained air following the obstruction and closure of the bronchus leading to the cavity. The authors agree with his conception of closure of cavities.

Cavities often close after hemoptysis. The clotted blood occludes the bronchus. With absorption of the contained air, there may be rapid closure of the cavity,

only to reopen again when the clot is absorbed and the bronchus again becomes patent. Figs. 54, 55, 56, 57 and 58 illustrate the above course.

**Sputum.**—One of the characteristic clinical findings in the caseous-pneumonic form of tuberculosis is sputum which usually reveals the presence of a con-



Fig. 46—The check-valve cavity noted in Fig. 45 three years later. The size of the cavity has not changed. The amount of fluid retained has increased considerably. There has been no change in size due to both a rapid absorption of gases through the walls of the cavity and a very narrow lumen of the obstructed bronchus that admits little entrance of gases into the cavity. It is in this type of cavity that spontaneous closure frequently occurs. See Fig. 46A.

siderable number of tubercle bacilli. From the very nature of the pathology this is to be expected. While the patient is in the acute phase and is sloughing out the caseated lung, the sputum is profuse. When the necrotic material has been expectorated and a cavity remains, the amount of sputum may diminish. It usually does not completely disappear until there has been an obliteration



of the cavity. Occasionally there may be some obstruction in the draining bronchus so that the sputum is not expectorated. This is merely a temporary affair. When the obstruction has been relieved, expectoration will be resumed. At other times the bronchial peristalsis may be so efficient that there is no urge on the patient's part to cough. The sputum is removed from the bronchial



Fig. 46A.—The check-valve cavity noted in Fig. 46 closes spontaneously. Twelve months have elapsed since the x-ray in Fig. 46. Note the narrowing of interspaces and shift of the trachea and upper mediastinum to the right.

tree and then taken into the stomach. Therefore a search for the sputum must be made in the contents of that organ. A fuller discussion of this is given elsewhere, on page B-45. The sputum from the case of true caseous-pneumonic tuberculosis is always positive for tubercle bacilli. The organisms are usually present in large numbers so that the Gaffky count is generally between five and ten. This high count of tubercle bacilli is one of the features which serves

to distinguish the caseous-pneumonic form of tuberculosis from the other types. In the exudative-productive tuberculosis there may be a fairly high concentration of tubercle bacilli at the onset of the process. Generally, however, the Gaffky count is not quite as high as in the caseous-pneumonic form. Fairly soon, however, the count in the exudative-productive tuberculosis begins to

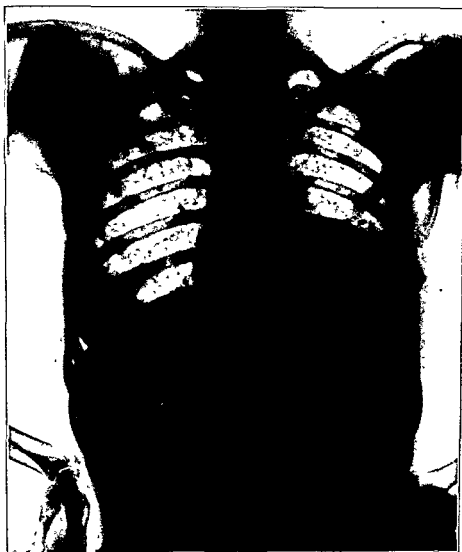


Fig 47—Figs 47 and 48 demonstrate the spontaneous collapse of a cavity in the right upper lobe with a resultant linear shadow that is ascribed to the collapsed walls of the bronchus leading to the cavity.

drop. The bacilli become less numerous and gradually tend to disappear. In the caseous-pneumonic form the sputum is persistently positive throughout the acute and chronic phases. The bacilli are found in undiminished concentration. It is this fact which makes caseous-pneumonic tuberculosis the malignant type of pulmonary disease.

**Prognosis.**—The prognosis in this type of tuberculosis is generally bad. The majority of patients within five years either have extension of their original pathology or are dead. Barnes and Barnes<sup>53</sup> state that 95 per cent. of their patients were dead within five years. Other workers have reported figures ranging between 60 per cent. and 70 per cent. for the same observations. We are

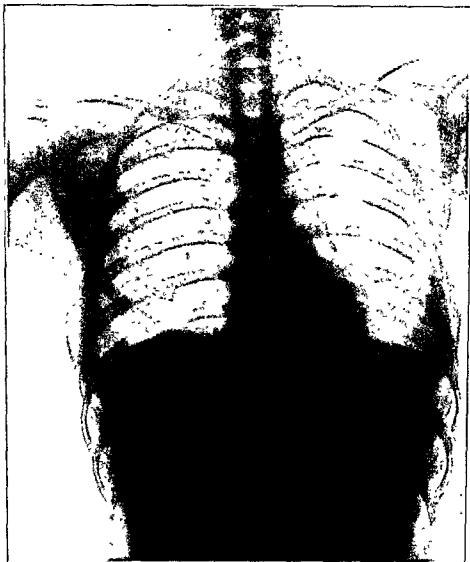


Fig. 48.—Note the linear shadow in the first interspace which marks the site of the large cavity seen in Fig. 47.

inclined to believe that the statistics reported by Barnes and Barnes are rather high. Observations among our own series would make us place the percentage of deaths well over 50, which, although a conservative estimate, is nevertheless a staggering figure and serves to impress upon us the seriousness of the problem. The reason for this unfortunate outcome in caseous-pneumonic tuberculosis is the presence of tubercle bacilli in the secretion originating in the involved portion

of the lung. As long as there are free bacilli in the bronchial tree there is always an opportunity present for bronchogenic extension of pathology. If there is a sudden spilling of a large amount of the secretion into a new area of the lung, one of the exudative forms of tuberculosis will result. It is very apt to be of the



Fig. 49.—An x-ray of a large cicatricial cavity in the right upper lobe. The patient died of a severe hemorrhage from large varices in the esophagus. No bacilli were found in the contents of the cavity at postmortem examination. The wall of the cavity was made up of scar tissue.

caseous type. If the spill is more in the nature of a dribble with small dosage in the reinfection, a more productive form of extension will be seen.

Occasionally a patient may be observed who has had a positive sputum for many years and yet has had no extension of pathology. One such patient was recently seen at Metropolitan Hospital. Fourteen years previously, following an attack of pneumonia and pleurisy on the right side, his sputum was found to be

positive. Ever since that time the patient has had a cough with expectoration. He felt well, however, and did his normal day's work as an accountant. The reason for his present hospital admission was troublesome hemorrhoids. Immediately after his chest was x-rayed, the patient was transferred from the



Fig. 50.—This is an example of the indurated thick wall cavity with stenosed bronchi. Due to the thick curvilinear wall there is no interchange of gases. A pneumonostomy was done in this case. One could look into the cavity. There was no visualization of patent bronchi.

surgical to the tuberculosis service. The patient had the end result of a caseous-pneumonic lesion in the right upper lobe. His trachea and mediastinum were drawn to the right. Many tubercle bacilli were found in his sputum. Cases such as this one with a sputum which we know to be positive during the fourteen year interval and which do not go on and spread are comparatively rare. The usual

outcome is disaster. Just why the above case should be spared is difficult to explain. The solution of this problem holds the fulfillment of the hope of cure that lies in the heart of every patient with caseous-pneumonic tuberculosis.

**Treatment.**—In any disease whose normal course when unaltered by extraneous influences leads to the death of the individual, the importance of therapy



Fig. 50A.—Multiple small cavities in the retracted parts of the left lung. Note the shift of the mediastinum to the left. A bronchogram (see Fig. 50B) outlines the course of the bronchi and the multiple small cavities.

looms large. Caseous-pneumonic tuberculosis is just such a disease. A review of the evidence presented in the preceding paragraph shows that the majority of patients with this form of pulmonary infection die of their tuberculosis. It is not immaterial, therefore, to expect that strenuous and heroic, and sometimes even hysterical attempts have been made to avoid this fatal ending. It is un-

fortunate, too, that the problem is further confused by the variegated clinical picture presented by the caseous-pneumonic form of pulmonary tuberculosis. Inability on the part of some phthisiologists to realize the continuity of the acute and the chronic forms of the disease has in part helped to complicate the problem. Failure to comprehend certain fundamentals of tissue response to tuberculous



Fig. 50B.—A bronchogram of the left lung previously demonstrated in Fig. 50A. Note the bronchiectasis appearance. Though some bronchiectasis is present the cavities are in the parenchyma of the lung. The bronchi are not dilated and empty abruptly into the cavity. The term bronchogenic cavities is a misnomer.

antigen has been another contributing factor. At the present time there seems to be considerable difference of opinion existing among various groups working in this field as to the proper mode of therapy. In the following pages we will present our own opinions with regard to therapy based on clinical and pathological experience gained at Metropolitan and Seaview Hospitals, New York.

If one analyzes the disasters that occur in caseous-pneumonic tuberculosis, it will be noted that they are due mainly to two causes: first, the train of events produced by the acute reaction of the tissue to tuberculous antigen, and second, the extension of disease with resultant loss of lung tissue and disturbance of lung physiology. In general, the first cause is a factor of the second, and the

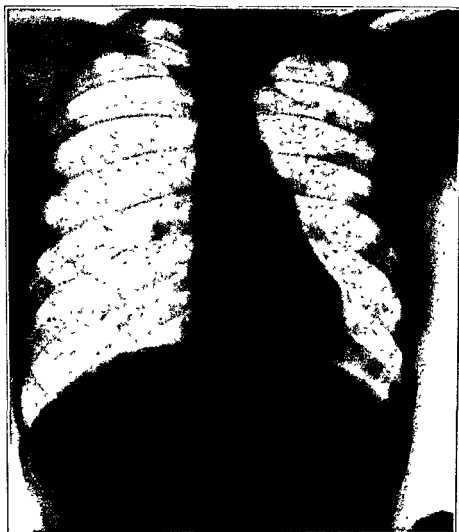


Fig. 51.—An x-ray demonstrating a check-valve cavity in the left upper lobe. Subsequent Figs 52 and 53 demonstrate the spontaneous closure and reopening of the cavity.

second is due solely to the presence of tubercle bacilli in the bronchial tree. It follows, therefore, that if one could clear the bronchial tree of all bacilli, the Gordian knot would be cut, bronchogenic spread would be completely done away with and the possibility of allergic reaction minimized. Our treatment therefore is directed toward the realization of this goal, namely, the disappearance of free bacilli from the bronchial tree. Irrespective of the subsidence of the acute



allergic aspect of the clinical picture, we consider our treatment a failure unless the sputum is negative for tubercle bacilli. Bitter experience has shown that rigid adherence to this dictum is the only hope of attainment of ultimate success in the treatment of this malignant form of tuberculosis.

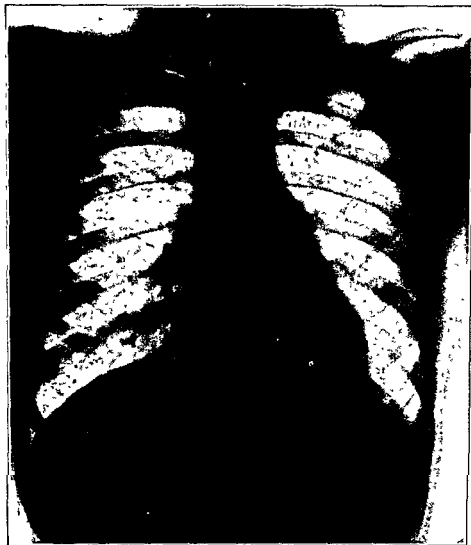


Fig. 52.—The spontaneous closure of a check-valve cavity in the left upper lobe after eight months of rest cure. The cavity in Fig. 51 has disappeared. With the closure of the cavity bacilli and symptoms disappeared.

**Therapy.**—A discussion of therapy in caseous-pneumonic tuberculosis may be divided into two parts, therapy in the *acute phase* and therapy in the *chronic phase* of the disease. We shall discuss first the treatment in the acute phase of the process. A consideration of the course of events in caseous-pneumonic tuberculosis shows that at the onset of the affair there occurs a tremendous over-irritation of lung tissue due usually to the aspiration of a massive dose of tuberculous antigen. As a result of this over-irritation there follow a death and

caseation of the lung tissue. The irritation takes place very soon after the contact between the tissue and the antigen. The symptoms appear concomitantly with the irritation. The death of the cells occurs sooner or later after the irritation has taken place. Those cells which have been most severely irritated succumb first, the less intensely irritated cells dying later. That portion of the

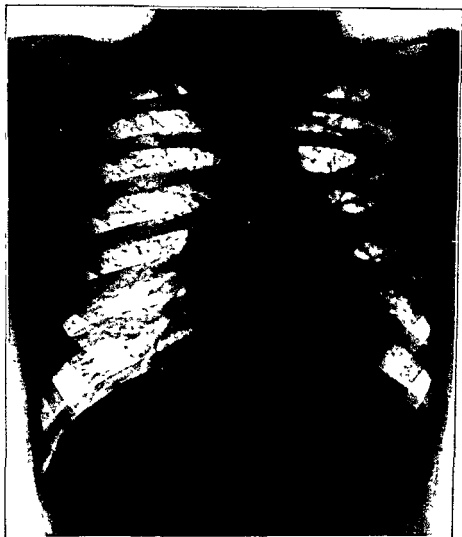


Fig 53—A complete re-expansion of a check-valve cavity after a lapse of three years. Compare Figs. 51 and 52. The cavity is in the same position, has the exact shape and only differs by a greater retention of fluid. Symptoms and positive sputum returned with the opening of the cavity.

lung which is at the margin of the affair, being stimulated by a sublethal dose of antigen, after precarious balancing on the brink of death recovers. A thorough realization of this sequence of events is essential for the rational treatment of the disease. From the above remarks several very important deductions may be made.

In the first place, allergic stimulation having already taken place, it is futile to institute any therapy which has as its object the return to normal of those cells which have already been fatally injured. In fact, it is quite conceivable that misplaced therapy of this sort can easily upset the delicate equilibrium of those cells which are just outside the line of demarcation between the living



Fig. 54.—Figs. 54 to 58 inclusive demonstrate the closure of a cavity following hemoptysis. The clotted blood obstructed the bronchus to the cavity and the cavity closed spontaneously only to reopen again when the clot was expectorated from the bronchus. This phenomenon occurred in the thick walled cavity seen in the right upper lobe. Note how little effect either size or thickened walls play in the closure of cavities.

and the dead. Should this take place, then the very aim of treatment is diverted and extension of disease instead of regression occurs. In spite of the simplicity of this logic there are many who believe that active therapy should be instituted in this early acute stage in order to prevent caseation and cavity formation. An insistence on this routine of therapy can only be explained by an ignorance of

the types of tissue reaction to tuberculous antigen and a peculiar attitude of mind which assumes full credit for any success but which refuses to take the blame for failure of treatment. As previously discussed, there are two forms of resolving acute tuberculosis, the benign exudative and the exudative productive. Both of these acute forms of tuberculosis have a sudden explosive onset similar

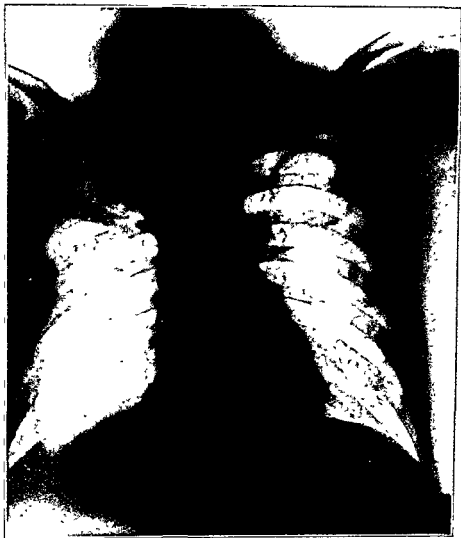


Fig. 55—The day of the hemoptysis. Note the density in the right upper lobe compared with Fig. 54. The right upper lobe appears to have become atelectatic.

to the caseous-pneumonic form. Unless these two types are clearly distinguished from the malignant caseous-pneumonic form, the attitude of mind which assumes credit for success will believe that the therapy was responsible for the resolution of the disease. The more proper way of thinking is that the disease in question resolved in spite of the therapy. It is probably this confusion which has led to the false attempts at therapy in the acute stage. The success which has been obtained with the resolving forms has led to similar attempts in the malignant

type. It has been our experience that nothing but failure greets the efforts to prevent death of tissue and caseation in the acute stage of true caseous-pneumonic tuberculosis.

It has been our practice in the past few years to treat patients in the *acute* stage of caseous-pneumonic tuberculosis by simple bed rest and symptomatic

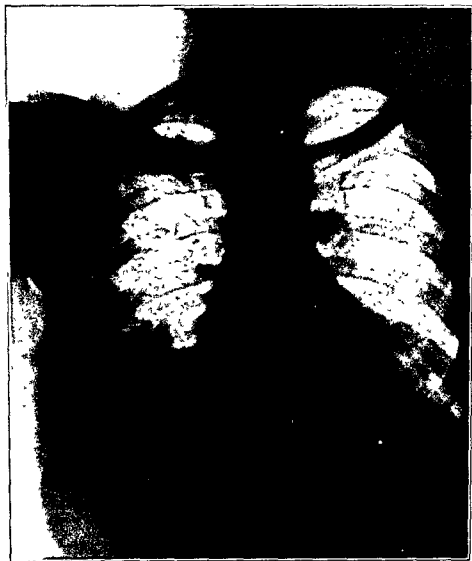


Fig. 56.—A month has elapsed since the taking of x-ray in Fig. 55. Note the disappearance of the huge cavity that has occupied almost all of the right upper lobe. There is a dense shadow in the first interspace, the remains of the collapsed cavity.

treatment. In this fashion two objectives are accomplished. In the first place, a period of bed rest allows the clinician the opportunity to differentiate between the resolving and the nonresolving forms of tuberculosis. Obviously, the patient who has a resolving tuberculosis is much better left alone than given pneumothorax treatments for three to five years as can so readily be done when the resolving and the nonresolving types are not differentiated. The second

objective gained by keeping the patient on simple bed rest in the acute stage is the opportunity it affords for whatever resolution is possible to take place.

Pneumothorax, which is frequently attempted at this stage of the disease, can, by its disturbance of circulation, not only retard resolution but also probably produce additional cell death. By its interference with the normal mechanism



Fig. 57.—Another month has elapsed. An attempt has been made to collapse the cavity in the left lung. Note the beginning of the re-expansion of the cavity in the right upper lobe (see Fig 56).

of lung drainage it frequently in the acute stage prevents proper expectoration of the copious sputum with the result that there is puddling of secretion and bronchogenic extension. Positive damage of still other character can be done by giving pneumothorax treatments at this time. This will be discussed later.

The prime indication in the acute stage is the avoidance of additional allergic stimulation and the avoidance of any act which might retard resolution or heal-

ing. Rest treatment at this time comes closer to fulfilling these premises than any other available mode of therapy.

The symptomatic treatment is simple. It necessitates the control of the cough and supplying an adequate amount of oxygen.

*Spontaneous Pneumothorax.*—Occasionally in the acute phase of caseous-pneumonic tuberculosis a spontaneous pneumothorax may occur. When this



Fig. 58.—The complete re-expansion of the cavity in the right upper lobe following a spontaneous closure when the bronchus leading to the cavity became obstructed by clotted blood. See Figs. 54, 55, 56 and 57.

takes place, profound changes in respiratory physiology are instituted which require treatment as mentioned above. As a general rule, the fluid which gathers in the pleural space in such a case is better left untouched. The presence of the fluid seems to act as a valve to close the opening. The removal of the fluid not only nullifies this effect, but also seems to stimulate the production of still more fluid. One of the few real indications for the aspiration of the exudate

is the embarrassment to lung ventilation which its presence may cause. Because of the hydrostatic pressure plus the increased air tension there may be a marked shifting of the mediastinum with a resultant cutting down of the air flow in the opposite lung. When the effect of this becomes severe and beyond control by the administration of the usual measures to combat anoxemia, fluid should be withdrawn.

With the subsidence of the acute allergic reaction and a sloughing out of the caseous material, the patient passes out of the acute phase of caseous pneumonic tuberculosis. It is now that the reparative side of the affair begins to assert itself. With the production of scar tissue an attempt is made by the body to replace the highly specialized lung tissue that has been destroyed by the caseation. Unfortunately the dead space is not filled by granulation tissue. It is merely lined by a granulation tissue, tuberculous in nature, from which there is a constant shedding of tubercle bacilli. Inasmuch as this area is in direct communication with the bronchus, the germs have free egress and are found in the sputum. Ample opportunity is likewise offered for a bronchogenic spread for the patient now is his own source of bacilli without the necessity for outside contact. The caseous-pneumonia has healed but in healing has left a bad end result, an end result which bathes the bronchial tree system with free tubercle bacilli and subjects the lung to the constant danger of reinfection. It is this bad mechanical end result which our therapy must now attempt to correct.

There are two methods whereby the clinician may cope with the problem that presents itself in the end stage of caseous-pneumonic tuberculosis. Inasmuch as the danger lies in the presence of free tubercle bacilli in the bronchial tree, one may attempt either to make the tissue of the host live amicably with the tubercle bacilli or to cause the disappearance of free bacilli from the bronchial tree. At the present time the latter course is the method of choice. Since the whole affair is the result of a bad mechanical end result, it follows that the method of attack is a correction of this mechanical defect or some other mechanistic action whereby its effect can be nullified. To fulfill the former requisite predicates the restitution of the cavitated lung to its normal *status quo*. Obviously this is impossible. To fulfill the latter requirement predicates a thorough understanding of the physiology of lung functions and especially of the principles of bronchial drainage. Unfortunately our knowledge regarding these fundamentals is still somewhat vague and sketchy. As a result our attempts in this direction are apt to be blind and groping and sometimes even bungling. However, the successful culmination of the attempts at therapy can be fairly accurately gaged by the disappearance of free bacilli from the bronchial tree. Therefore, irrespective of how the result is accomplished, once the true sputum becomes negative and remains negative for tubercle bacilli the efforts at therapy in caseous-pneumonic tuberculosis may be considered successful. With the clarifications of our knowledge regarding the mechanism whereby this result is accomplished, the therapeutic efforts will become more logical and exact. To this end further investigation of pulmonary physiology is urgently needed.



In order to accomplish the purpose of treatment and free the bronchial tree of bacilli, all that is necessary is to bottle up the organisms at their source so that they are unable to escape and spill through the remainder of the lung. Obviously, the most logical method of doing this would be to artificially produce a complete obstruction in the bronchus supplying the involved area. Unfortunately this is technically impossible at the present time. Bronchial obstruction almost invariably leads to lung suppuration usually of an anaerobic type due to the ability of normally present aerobic organisms to become facultative anaerobes. When this takes place, the patient is much sicker than previously.

At the present time our mode of attack is a very roundabout and inefficient one and consists in the application of procedures variously known as collapse or compression therapy. By means of these purely mechanical attempts the phthisiologist tries to nullify the bad mechanical end result of caseous-pneumonic tuberculosis and thus obtain a negative sputum. In these procedures the manipulation is made on the gross lung with the hope that the desired result is obtained at the site of the disease. Exactly how this result is obtained is not well understood.

*Resting*.—At one time it was thought that the resting of the lung was the important point. Extension of disease in a collapsed lung readily shows the fallacy of this view. The rôle that actual compression plays is problematical. From the point of view of compression by pneumothorax, it is doubtful whether this can ever occur, except by the valve effect of a spontaneous pneumothorax or the continued high pressure in an artificial pneumothorax with a very thick pleura. With the permeability of the pleura that is almost always present, any increase in pressure above the normal only serves to make the gas diffuse out faster. Frequent manometric readings following so called higher tension pneumothorax have shown that the pressure drops to zero within one hour and is usually on the negative side within two hours.

*Collapse Therapy*.—The effect that collapse therapy has on the bronchi is not so easily disposed of. One might suspect that collapse therapy will so distort and block the bronchi that the bacilli are entrapped in the cavities and are unable to escape. It is quite conceivable that some slight distortion might be established which would readily admit of plugging with thick tenacious mucus. Another explanation is that the collapse of the lung interferes with the normal peristaltic action of the bronchi in expelling sputum. Where the expulsive cough mechanism is seriously interfered with, as usually takes place in any collapse therapy, this peristaltic action is extremely important. To interfere with it is equivalent to entrapping the organism inasmuch as they cannot be coughed up or otherwise expelled. In all probability the mechanism of obtaining a negative sputum is a combination of distortion of the bronchi plus a disturbance of their normal peristaltic action.

It is upon this shifty and unstable foundation that the phthisiologist builds his therapeutic attempts. The procedure that is employed will be limited merely by the physiological tolerance of the patient and the mechanical ingenuity of the therapist. The usual procedure that is first attempted is artificial pneumothorax. By means of this step maximum disturbances in bronchial physiology may be established with a minimum of inconvenience and risk on the patient's

part. Inasmuch as the technical details of this as well as other collapse procedures will be described in other chapters, it is not the aim of the writers to discuss these details in this section. It would not be amiss, however, to amplify a remark that has been previously made, namely, that it may be futile and even dangerous to attempt this form of therapy in the acute phase of caseous-pneumonic tuberculosis. The futility of the treatment has been discussed in the section on the treatment of the acute phase of caseous-pneumonic tuberculosis. The danger of this treatment in the acute stage, which was merely alluded to, lies in the fact that some of the patients so treated develop a spontaneous pneumothorax, superimposed on the artificial pneumothorax.

*Adhesions.*—Unfortunately, after the acute phase of the disease has passed there may be formed between the visceral and parietal layers dense strong adhesions which prevent adequate distortion of the bronchi by this form of collapse therapy. When this occurs, the future procedure will be based on the technical skill and the mechanical ingenuity of the manipulator. At times it is possible to cut the adhesion which by its guy rope effect is maintaining the normal bronchial relationship to the diseased area of the lung. In order to advise this treatment there must always be kept in mind the relationship of the bronchi and the effect that the release of adhesions will have on this vital factor. These adhesions may be divided by either closed or open manipulation, the closed pneumolysis or Jacobaeus operation being more usually performed because of its relative simplicity. At times the character of the adhesions presents insurmountable technical barriers which prevent their severance. At other times the adhesions between the visceral and parietal pleural layers are so extensive that pneumothorax cannot be induced at all. When such is the case, and the sputum remains positive, some other mechanical attempt must be made. Here again the skill and ingenuity of the operator coupled with his knowledge of bronchial physiology will determine the course that is to be followed. As might be readily imagined, many and various procedures have been performed. Extrapleural thoracoplasty or one of its modifications has up to now been the mainstay of the phthisiologist in the further pursuance of collapse therapy. Apicolysis has also been utilized in some instances. At other times a combination of thoracoplasty and pneumothorax has been tried. In each case it must be realized that the therapy in all probability is directed toward the distortion of the bronchial tree to the end that the tubercle bacilli are entrapped at the site of disease. With this in view we believe that the routine use of the thoracoplasty operation will be superseded by less groping and more exact measures to reach the goal of therapy—a negative sputum. Whatever technical detail is executed should be directed at the bronchi rather than toward the collapse or compression of the lung. The latter in most instances is merely incidental to the former.

Where the source of bacilli is in both lungs, the problem of therapy assumes much more serious aspects. Since the goal of therapy is a negative sputum, it is obviously ridiculous to perform any mechanical manipulation on one lung without attempting to shut off the supply of bacilli from the opposite lung. Unfortunately, at the present time, our modes of treatment are so crude that in order to have any effect on the diseased area the entire lung is generally affected

by the manipulation. To attempt such drastic handling of both lungs would, in most instances, diminish the respiratory function of the patient to such an extent as to make life untenable. The patient might be cured of his caseous-pneumonic tuberculosis but would surely die of asphyxia. For this reason in only comparatively few cases has bilateral collapse or rather distortion therapy been attempted and then only over relatively localized areas where selective collapse can be obtained.

*Bilateral Pathology.*—Unfortunately, many cases of tuberculosis are seen that have their caseous-pneumonic pathology distributed bilaterally, and distributed in such a fashion as to make bilateral collapse therapy inadvisable for reasons that have been enunciated above. If nothing is done for these blighted individuals, they are doomed to a comparatively early death. As has been previously discussed, the real danger arises not so much from the productive tissue response but rather from the overirritation of the lung tissue due to massive stimulation by the aspirated tuberculous antigen. With each fresh aspiration there is a new hyperirritation which is reflected both clinically by an exacerbation of the acute toxic symptoms and pathologically by an extension of the exudative reaction, usually of a caseous nature. If this hypersensitivity of the tissue to tuberculous antigen could be eliminated the acute allergic response would disappear. No longer would the patient be sick and toxic nor would acute exudative reactions take place in the lung. There would remain merely the productive response which, as will be shown in the section on chronic productive tuberculosis, is relatively innocuous. The ideal condition, of course, would be to produce a state of affairs in which the tissue of the host is entirely refractile to tubercle bacilli. The albino rat is an example of this utopia. Perhaps this goal will eventually be reached. At the present time, however, we have been content to merely tamper with the hypersensitivity of the host in an attempt to eliminate the acute allergic manifestations. Our efforts in this direction have extended over a period of more than two years. The results to date have been sufficiently encouraging to warrant the continuation of this form of therapy.

In view of our ignorance concerning the basic principles underlying problems of hypersensitivity of tissue in general, and the hypersensitivity of tissue to tuberculous antigen in particular, it is somewhat difficult to explain the happenings as observed clinically. A few details, however, are fairly well established. A high sensitivity is detrimental to the host whereas a low sensitivity which leads to the relatively innocuous productive response in no way interferes with the ability of the host to localize the bacilli. With decreasing sensitivity of tissue, larger and larger doses of tubercle bacilli must be aspirated in order to cause exudative lung reaction. As a result, once the patient has become desensitized, the majority of the tissue reactions to aspirated bacilli are of a productive nature. This productive form of tuberculosis is preferable to the caseous-pneumonic types which might have occurred in a more sensitive individual. The method of desensitization is given under tuberculin therapy.

*Summary.*—In the preceding pages we have attempted to outline our ideas of therapy in caseous-pneumonic tuberculosis. During the acute phase bed rest offers the best opportunity for recovery. With the sloughing out of the caseous

material and the appearance of the chronic phase of the disease, the phthisiologist must attempt to free the sputum of tubercle bacilli. Unless this is accomplished the treatment will not be truly successful. At the present time mechanical attempts such as pneumothorax, thoracoplasty or various other procedures, offer the best hope. Where these steps are inadvisable, the only other available mode of therapy is some other means, such as desensitization, whereby the tissue can be made more tolerant toward the tubercle bacillus.

### CHRONIC PRODUCTIVE TUBERCULOSIS.

Chronic productive tuberculosis is decidedly different from the exudative forms. It comprises the large ambulatory group of tuberculous patients. The patients are rarely very ill. The onset is insidious and the diagnosis difficult in the early stages. The greatest number are recognized as tuberculous in the late stages and could easily be overlooked even then were it not for the roentgenogram. The usual duration of the disease is about twenty years. If one assumes that most adult infections occur between sixteen and twenty years of age, the fact that clinical manifestations of productive tuberculosis appear in our institutions during the fourth decade confirms this long duration of disease. Productive pulmonary tuberculosis is a chronic disease and runs a slow course over a long period of time.

**Pathology.**—If the superinfecting dose is small and the allergic reaction slight, there results a low-grade productive response consisting of epithelioid, giant and round cells. The process, according to Aschoff<sup>55</sup> and his pupils, starts in the bronchial tree at the junction of the terminal bronchioles. With occlusion of the bronchus there is a resultant atelectasis of the associated alveoli. The adjacent alveoli are soon involved and we have the form of acinous productive tuberculosis described by Aschoff. Multiple, closely placed areas of the lung may be involved, giving the organ a cirrhotic appearance. This cirrhotic type is not frequently seen. The usual form is the disseminated acinous-nodular productive tuberculosis. When extensive, the disease is sometimes mistaken for a blood-stream infection. The irregularity in size and shape of the lesions and the unequal distribution differentiate it from a blood-stream infection. Adjacent foci may emerge and caseation occur with resultant small cavity formation. Following caseation, infection by aspiration takes place and the spread is bronchogenic.

Productive tuberculosis is relatively avascular. There is, therefore, little absorption of toxins. This accounts for the few subjective symptoms. Most cases in the minimal stage are usually diagnosed by accident. Whatever slight symptoms that are complained of occur during the beginning period of reinfection. The symptoms rapidly disappear and are usually not noted by the patients as they continue their normal routine in life.

**Clinical Picture.**—The clinical picture depends a great deal on the extent of the disease. During the early stage symptoms and physical signs are very scant. Most early infections are overlooked and few cases would be recognized were it not for the timely and frequent appearance of hemoptysis. Symptoms of toxemia do occur with the beginning of infection. Because of the avascular form of the pathology the changes from the normal are so slight that the patient

rarely takes cognizance of these alterations. Rises in temperature and pulse rate do occur but are seldom noted. Cough and expectoration may not occur during this early stage. Of the symptoms of toxemia, fatigue is often complained of. Hemoptysis is quite a frequent happening. When this occurs, the patient seeks aid and a diagnosis is made.

In the advancing stages symptoms are more pronounced. With progression of the infection, emphysema occurs and dyspnea becomes the most common complaint. There may also be an associated chronic bronchitis so that the picture frequently resembles anything but pulmonary tuberculosis. We now see the large group of chronic coughers who are diagnosed as anything from a cigarette cougher to a chronic asthmatic. Hemoptysis in this stage of the disease is also a frequent happening.

Because of the anoxemia that occurs in the late stages the patients have an almost characteristic appearance. They are usually underweight and have flat-shaped chests with a rather pot-shaped abdomen. There is a general lack of muscle tone. The scapulae have a winged-like appearance. Though the shape of the chest has not usually the barrel appearance of the emphysematous patient, the intercostal spaces are very wide. A pale cyanosis is present, especially after the least exertion. Due to the anoxemia in the late stages extreme fatigue becomes the chief complaint. There is usually an associated depression which we believe is also caused by the anoxemia.

#### PHYSICAL FINDINGS.

In the early stages the physical examination may reveal no abnormal findings. In fact, even in the advanced stages there may be a paucity of abnormal findings. Negative physical findings should not rule out pulmonary tuberculosis. Because of the associated compensatory emphysema there may be no perceptible change in breath sounds. When the infiltration is close to the surface of the lungs, bronchovesicular breathing and fine high-pitched moist râles may be heard. As a rule the physical signs are not commensurate with the extent of the x-ray pathology. In the minimal stage the compensatory emphysema heard over the upper lobe should make one suspicious of underlying disease. As the infection extends more abnormal findings are heard but never to the extent that they occur in the other forms of pulmonary tuberculosis. With the complicating emphysema and chronic bronchitis the diagnosis may be confused with that of a mild asthma. Sibilant and sonorous râles frequently add to the confusion. All forms of emphysema and chronic bronchitis should be looked upon suspiciously as chronic productive tuberculosis especially where there has been a hint of blood-spitting.

*Summarizing, physical findings in the early stages are scant. Moist râles at an apex or compensatory emphysema over an upper lobe are suggestive of an early infection. In the advanced stages abnormal findings are also scant. Emphysema and signs of subacute bronchitis may frequently mask the underlying disease.*

**Sputum Examination.**—Demonstrating tubercle bacilli in the sputum is the most complete and incontrovertible evidence of the existence of tuberculosis

in the lung. It is most unfortunate that in this type in which diagnosis is so difficult tubercle bacilli are infrequently found in the early and even moderately advanced stages. It is not uncommon for the sputum to be reported negative for tubercle bacilli in as many as twenty examinations before they are found once. This absence of tubercle bacilli after many examinations of the sputum frequently misleads the practitioner. Further confusion occurs because the tubercle bacilli are found in low Gaffky counts and a careless examiner will report the specimen negative. Concentrated sputum examination should be advised. The maxim that scanty sputum and negative demonstration of tubercle bacilli does not rule out tuberculosis whereas copious expectoration with the absence of tubercle bacilli should suggest another form of pulmonary disease, does not necessarily hold in the chronic productive tuberculosis. In the late stages of the disease, because of the emphysema and chronic bronchitis, expectoration may be very copious and tubercle bacilli are still difficult to demonstrate. Terminally, after caseation of the individual lesions, tubercle bacilli become plentiful and very easy to find.

**X-ray.**—The shadows in the roentgenogram in chronic productive tuberculosis have a characteristic appearance. No more do we see the large irregular exudative shadows involving a part or whole of a lobe or lung. The shadows are small and disseminated with an acinous distribution which gives the lung a peculiar mottled appearance in the roentgenogram.

The early infection occurs in the apex of the lung and spreads slowly down the lung to the base. In the course of this extension the upper lobe of the contralateral lung also becomes involved and the process again begins to descend down to the base. This widely disseminated nodular appearance simulates the miliary form of tuberculosis. The irregularity in size and shape of the nodules and the unequal bilateral distribution differentiates it from miliary tuberculosis. The density of these small nodular areas may be greater than the ribs but is much less than the calcified areas associated with first infections. Frequently there is a conglomeration of these small nodules so that they may attain the size of a cherry. With considerable fusion of these nodules the lung takes on a cirrhotic appearance. When the larger areas caseate there are resultant small cavities which give a honeycombed appearance in the roentgenogram.

The trachea rarely deviates from its normal position. In the advanced stages the complicating emphysema changes the shape of the thorax, the intercostal spaces becoming unusually wide. The new infiltrations can be recognized by their soft shadows and hazy margins.

Confusion in diagnosis may occur when a small cavity in an upper lobe seeds the remaining portion of the lung with small acinous lesions (see Fig. 36). At first glance the appearance is that of chronic productive tuberculosis but when the cavity is discovered we know that we have a caseous-pneumonic process and the lung must be collapsed immediately. Furthermore, the extension of the lesion in the above example is relatively rapid in contrast with the slow browsing down of infection in chronic productive tuberculosis.

**Clinical Course.**—From previous discussion we know the progression of the infection is slow. Years elapse before the disease extends down through both

lungs. We have emphasized the difficulty in early and even late recognition and pointed out the fact that patients come to the Clinic chiefly because of the complicating emphysema with its train of symptoms. Fortunately, this disease does not always progress and may stop in the minimal or moderately advanced stage.

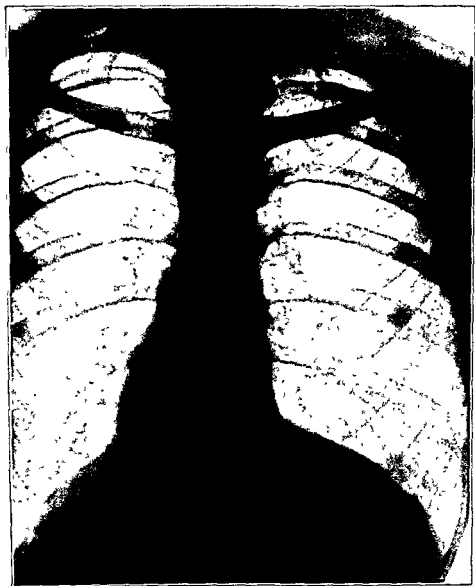


Fig. 59.—A diffuse acinous infiltration of productive tuberculosis in the right upper lobe.

A large number of these cases are accidentally found in contact examination or in case-finding campaigns.

The following case reports demonstrate how the disease may be stationary for many years:

CASE I.—A woman, age 39, was examined as a contact ten years ago. She had no complaints except for occasional cough with slight expectoration in the

morning. She felt well up to the time of examination. She worked hard, helping her husband in a retail store and attending to all her household duties.

Physical examination revealed some altered breathing, bronchovesicular in character, and moderately coarse moist râles over the upper half of the right upper lobe. An x-ray of her lungs revealed a disseminated lesion in the upper

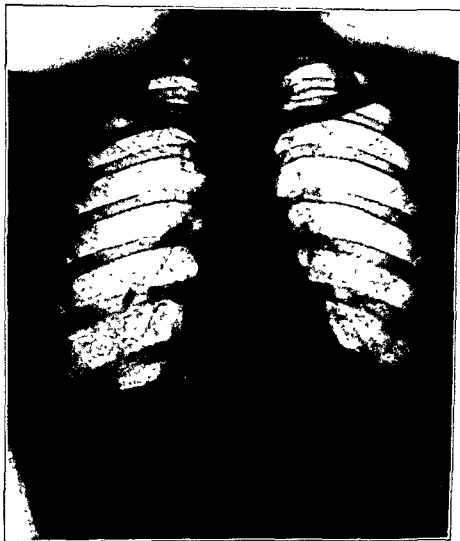


Fig. 60—An x-ray taken ten years following the x-ray in Fig. 59. There has been no change in physical findings. The patient, except for a short rest, has been carrying on these past ten years.

half of the right lung. Tubercle bacilli were searched for and demonstrated in small numbers in her sputum. The patient had no temperature and her pulse rate was normal. A diagnosis was made of moderately advanced tuberculosis and she was kept at rest for six months. She gained considerable weight. There was no change in her findings after the lapse of the six months. Sputum examinations revealed occasional tubercle bacilli. Financial reverses changed our



plans for treatment and this lady had to return home and help both in business and household. There has been no change in the situation in the past ten years. Within the first year bacilli disappeared from her sputum. There has been no alteration in physical signs these ten years. Serial x-ray examinations disclosed no change in character and extent of lesion over a period of ten years. Fig. 59 is an x-ray in 1923 and Fig. 60 taken in 1933.

Had the patient not been examined as a contact she would not have been aware of her tuberculosis. Apparently the course of the disease was not affected over the ten years by her continued occupation. In the past few years the whole responsibility for support of the family has fallen on her shoulders. Her pulmonary lesion has remained stationary.

Very frequently this type of pulmonary tuberculosis is kept at the sanatorium or tuberculosis center for years because of the persistence of physical findings. We believe that at the discovery of productive tuberculosis the patients should be given a period of rest and then returned to their normal routine. We do recommend that they be kept under observation. Whenever there is an extension, they should be sent to the sanatorium for a rest period and when the symptoms abate, they may be sent back home to take up their usual duties.

The next case is that of a healed chronic productive tuberculosis.

CASE II.—The patient, a white male, age 39, having heard a lecture on the frequency of the occurrence of pulmonary tuberculosis, came to the Clinic because of a persistent cold the past month. His history suggested a subacute tracheo-bronchitis following a nasopharyngeal infection which began a month previously.

The physical findings were scant and suggested the probability of a tracheo-bronchitis. A few musical râles were heard over both upper lobes. Because of the constant preaching in our Clinic that negative physical findings should not rule out pulmonary tuberculosis, the patient was x-rayed.

The roentgenogram disclosed a minimal lesion in the left upper lobe. The character of the pathology was that of a disseminated acinous-nodose form of productive tuberculosis. The sharply demarcated nodules suggested a lesion of long standing. The sputum examination was repeatedly negative for the finding of tubercle bacilli.

The patient had an important position and we decided that his tuberculosis was arrested. Also, because of the slow progression in this form of infection we thought he would risk little if he continued on with his routine provided he was frequently checked up. The patient has been at work the past three years. During this period he has had his badly infected tonsils removed. His roentgenogram shows no change, as can be seen in Figs. 61 and 62 which represent a span of over three years. This is the type of pulmonary tuberculosis in which grave injustice may be done to patients by sending them away and disrupting their careers. In the past, before qualitative recognition was used, the above case would have been diagnosed as incipient tuberculosis and sent away immediately.

The above cases demonstrate that chronic productive tuberculosis frequently stops progressing and becomes arrested. The usual course is a slow extension. Irrespective of what is done the disease progresses even in the absence of any

symptoms. We were fortunate in a contact examination of finding just such a case in a youngster and following it the past seven years.

CASE XIV.—A young white boy, 11 years of age, was seen at the Clinic six years ago because of contact with an open case of pulmonary tuberculosis.

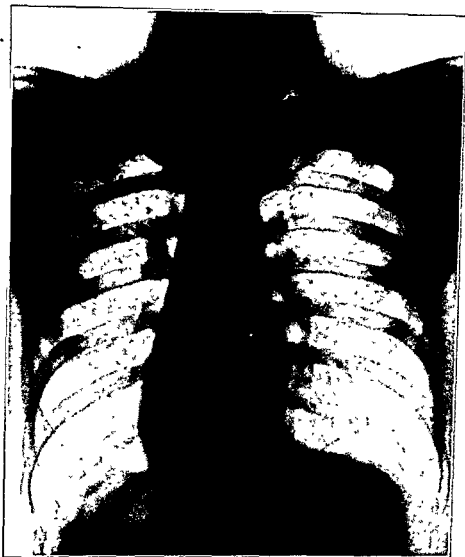


Fig 61—A minimal healed productive tuberculosis in the left upper lobe. The patient, having attended a lecture on tuberculosis, insisted on examination for pulmonary tuberculosis. Negative physical examination. Patient was allowed to continue usual routine.

Physical examination revealed no abnormal findings. The roentgenogram (Fig. 63) disclosed a minimal infiltration in the apex of the left upper lobe. The character of the lesion was chronic-productive. There was no cough or expectoration and therefore no sputum to be examined for tubercle bacilli. The tuberculin skin reaction was positive (von Pirquet with old tuberculin). The weight of the patient was 92 pounds. Temperature and pulse rate were in the normal range.

The patient was given complete rest at home for a period of six months. He added eleven pounds in weight, appeared in good health and had no complaints. Physical examination revealed no abnormal findings. He was allowed to return to school. Arrangements were made for him to have an afternoon nap and it was impressed on his family that he was to go to bed early.

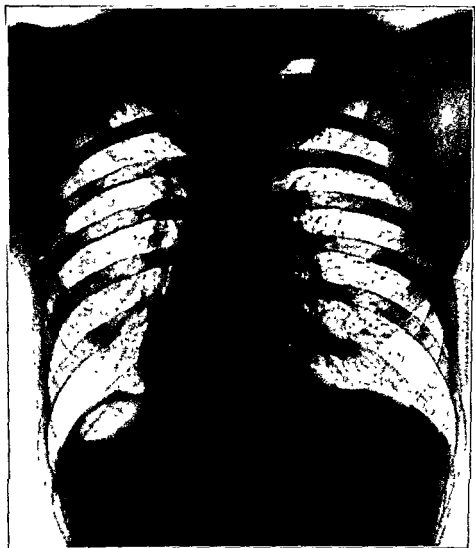


Fig. 62.—A span of three years since the x-ray in Fig. 61. There has been no change in the x-ray. The patient has been at work the past three years.

The patient returned to the Clinic for examinations at frequent intervals and apparently did well. A detailed examination was made 15 months later. He had no complaints. His weight had increased again, showing a gain of twenty-four pounds in the fifteen-month interval. Temperature and pulse rate were in the normal range. Physical examination was negative for any abnormal findings. The x-ray (Fig. 64) revealed an increase in the lesion. The process had extended from the apex to lower border of the second rib. In spite of the absence of

symptoms or signs there had been an increase in the extent of pathology. We decided to send the youngster to a sanatorium. This was done. He was put to bed but after a few weeks of normal temperature and pulse rate and no symptoms was put on graded exercise. In spite of an absence of symptoms and an increase in weight the process continued to extend.

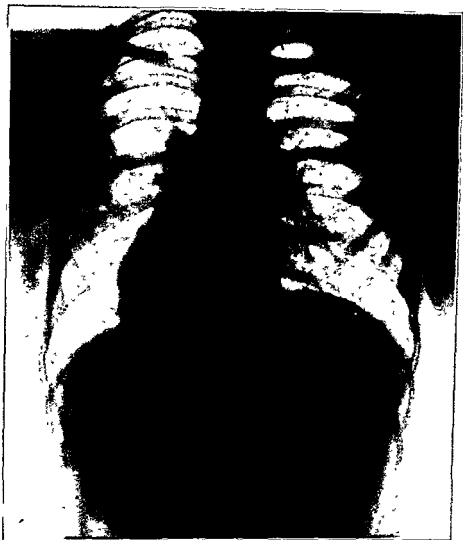


Fig. 63.—Figs 63 to 68 inclusive demonstrate the pathogenesis of chronic productive tuberculosis. Fig 63 is an x-ray of a boy 11 years of age examined because of contact with an open case of tuberculosis. Physical examination revealed no abnormal findings. The boy had no symptoms. In the apex of the left upper lobe a minimal conglomeration of acinous infiltration was noted.

The boy did not like his routine and the family removed the youngster against advice. We lost track of him until ten months later when he returned to the clinic for an examination. Again there were no complaints, no cough, no expectoration. His weight had again increased. X-ray (Fig. 65) examination showed further progression of the pathology. It now extended down to the third rib.

The mother informed us that he had won some Track medals at school and was considered the best all-around athlete in the school! Again we advised sanatorium care which advice the family refused to obey. The youngster was carefully watched and in spite of the careful vigilance there appeared the same slow

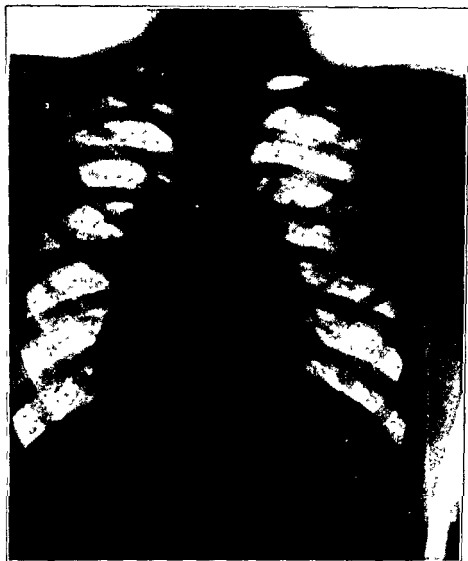


Fig. 64—Following a six months rest in bed the boy was sent back to school. There were no complaints. Physical examination was always negative. The boy added 24 pounds of weight. An x-ray taken 15 months following the one seen in Fig. 63 shows an extension of the tuberculosis, extending now from the left apex to the second anterior rib.

extension in the roentgenogram (Fig. 66). The interval between x-rays was eight months. The process was now past the third rib in the left lung.

Between 1930 and 1933 the process remained stationary (Figs. 67 and 68). At his last examination he still complained of no symptoms. His examination revealed no abnormal findings and his weight in six years had increased from

ninety-two to a hundred and thirty pounds. He had left school and had worked with his father. The occupation required his going in and out of a large refrigerator. In spite of hard work and the rapid changes in temperature the disease had stopped extending.

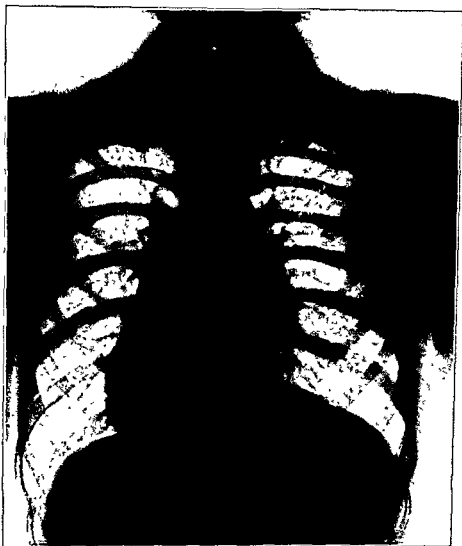


Fig. 65—When the spread of disease was noted in Fig. 64 the boy was sent to a sanatorium. After a short rest during which there were no abnormal findings the child was allowed full liberties. The parents removed the youngster from the sanatorium and he was sent back to school. At the end of a year his weight again increased. He had no complaints. Physical examination was negative. The disease had again spread as can be noted in Fig. 65.

The above case, an excellent demonstration of the slow course of this disease, shows how productive tuberculosis may extend in spite of the absence of both symptoms and physical findings. We can now understand how chronic productive tuberculosis can spread and not be recognized until it has invaded both

lungs. It is also interesting to note that treatment had little effect on the progress of the disease. The extension stopped under the most unfavorable conditions. Should this lesion progress, it will take a great many years before this youngster will be incapacitated. This explains the fact that most cases of chronic productive tuberculosis reach the clinic and hospital around the fourth decade.

Figs. 69 and 70 show more advanced stages of the disease.

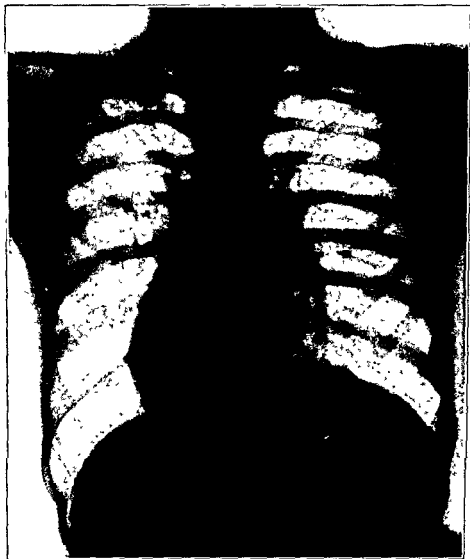


Fig. 66—Further extension of the disease with no symptoms and physical findings. Eight months have elapsed since the taking of the x-ray in Fig. 65.

From the above cases we can follow the slow extension of the productive type of tuberculosis. Because of the absence of symptoms in the early stages diagnosis is usually accidental. In the more advanced stages hemoptysis and complications lead to the diagnosis. Emphysema and chronic bronchitis are the common complications. Tuberculosis of the larynx is also a frequent complication with frequent infection of the mucous membrane of the mouth and pharynx.

Most tuberculous infections of the tongue are seen with the chronic productive type of tuberculosis. Tuberculosis of the intestines is also commonly encountered in the late stages and may be the cause of the presenting symptoms.

The terminal stage is associated with acute reactions around most of the nodules and mixed productive and caseous-pneumonic lesions are seen at the postmortem table.

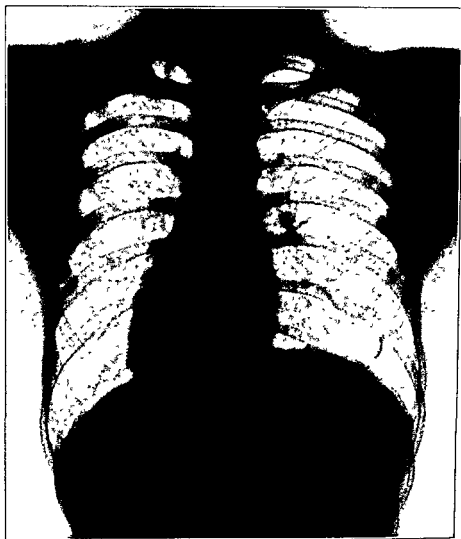
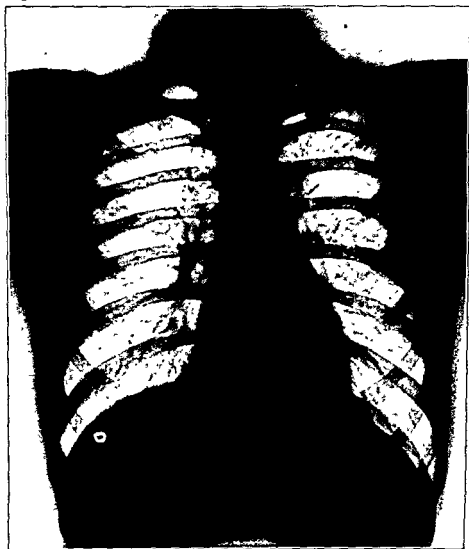


Fig. 67.—An x-ray one year after Fig. 66. The boy's weight had increased from 92 to 130 pounds. There has been a slight extension of the disease.

**Diagnosis.**—Because of lack of both symptoms and abnormal physical findings early diagnosis is extremely difficult. Even in the advanced stages both symptoms and signs are not plentiful. Emphysema is usually the complaint for which the patient reports to the physician. The increasing dyspnea and the associated fatigue suggest ill health and no one is more surprised than the patient when the diagnosis of tuberculosis is made.



Were it not for the frequent occurrence of hemoptysis but very few early cases would be discovered. In the early stages negative physical examination is of little value. Only positive findings are of importance and the slightest changes in the percussion note and in breath sounds on auscultation should make one suspicious of disease. There is no need to discuss the value of dullness versus



*Fig. 68.—Three years more have elapsed since Fig. 67. The patient is still free of symptoms. The boy has left school and is at work. For the first time no extension of the disease has been noted*

bronchovesicular breathing in the upper lobes or the altered breath sounds compared with the finding of moist râles. With any of the above changes the lungs should be further investigated.

The difficulty in demonstrating tubercle bacilli in the sputum has been discussed and their absence should not influence the diagnosis. The x-ray is of extreme value in diagnosis. Because of the sharp contrasts made possible by

the aerated pulmonary tissues, the diffuse small nodules can be easily seen in the roentgenogram.

In the advanced stages the discomfiture of the complications are complained of more than the symptoms due to the process in the lungs. Dysphagia because of a complicating laryngitis or abdominal pain due to a stenosed cecum are two

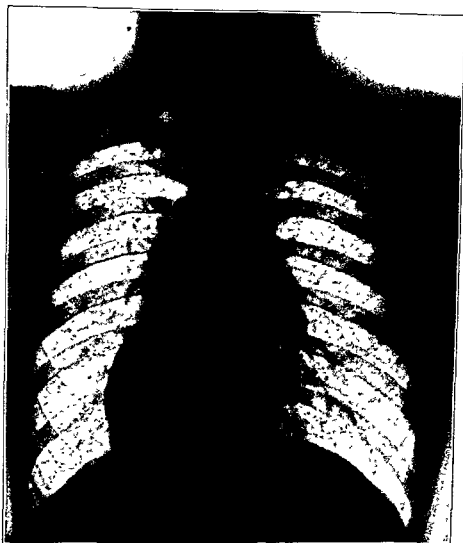


Fig 69—A moderately advanced stage of the chronic productive tuberculosis accidentally discovered in an examination as a contact.

frequent complications. Tuberculosis of the mucous membrane of the mouth and pharynx may complicate advanced productive tuberculosis.

**Treatment.**—Treatment in the early stages is very simple. With a moderate amount of rest the symptoms rapidly disappear and weight is quickly accumulated. The difficulty in demonstrating tubercle bacilli has been previously discussed. With loss of symptoms, absence of tubercle bacilli in the sputum and increase in weight, the patient, after a short stay in the sanatorium, is discharged

as an arrested case. We can now understand why so many sanatoria prefer this type of patient. They have no fatalities to report and unless a caseous-pneumonic type is accidentally admitted, may go on for years with no record of deaths. They point with pride to the large number of improved cases. These patients could have been treated at home. Because of the few tubercle bacilli expectorated they are of little menace to their family and are not bacilli carriers as are the caseous-

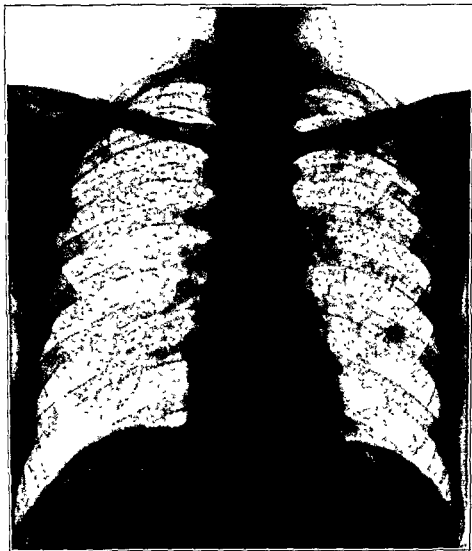


Fig. 70.—A far-advanced stage of the chronic productive tuberculosis.

pneumonic types of tuberculosis. In the last decade patients with minimal productive tuberculosis have been given all the advantages of the sanatorium while the caseous-pneumonic cases with a fatal prognosis have been left home to infect the remaining members of the family and to die.

We are not to be misunderstood. Rest treatment should be insisted upon and should be arranged for at home or away at the sanatorium. Our criticism is with the municipal, county, state and semi-charitable institutions that select the

so-called "incipient tuberculosis." Minimal chronic productive tuberculosis forms almost all of the latter group. Furthermore, the patients have to be afebrile and have no complications. They are on the path to recovery before they reach the sanatorium, while there are insufficient accommodations for the really sick caseous-pneumonic case. So much for the indigent. Those that can afford to go away may be sent to the sanatorium but only for a period of time necessary to free them of symptoms.

In the case reports we have seen that rest often has little effect on the course of the disease and progression continues in spite of all precautions against the extension of the infection. In the majority of the cases the progress of the disease is slow and a long period of time elapses before the patients are incapacitated. Our plan of treatment has been to leave this group of patients alone while they are symptom-free even in spite of slight extension of pathology as can be seen in serial x-ray examination. If the course of the disease extends over a period of twenty years the patients are much better off following their routine of life than to be exiled to a tuberculosis center for years.

It is not uncommon for a patient to go to a sanatorium or tuberculosis center with a minimal lesion only to improve clinically but be kept on because of continual extension of disease as seen in the roentgenogram. With normal or scant physical findings, with no symptoms and with sustained gain in weight, these patients hike over hill and dale only to find a further extension in the next x-ray examination. They are put back to bed. So this procedure is continued again and again over the years. These patients are better off at home at their occupation and get along under simple guidance. More rest than for the normal individual should be insisted upon. Recognition of new invasion is important. This can be done by a continual check-up of temperature and pulse rate. Increases should be regarded as danger signals. A short time to bed and the symptoms again subside. These patients should then be sent back to their previous normal routine.

As the disease extends the treatment is more difficult. The complicating emphysema rather than the productive tuberculosis must be dealt with. Warm climatic treatment is most important. The patients do very well in summer and complain bitterly of the wind and cold during the winter. There is nothing to do for the far-advanced cases except to treat them symptomatically. With emphysema and anoxemia, cardiac failure becomes a serious complication.

There is only one indication for collapse therapy. In some cases there is a conglomeration of the nodular masses with resultant small cavity formation. When this occurs, an attempt should be made to collapse the lung by pneumothorax. Should inflation *not* be possible, the indications for other forms of surgery are the same as in the caseous-pneumonic tuberculosis. Collapse therapy is done only for the closure of the cavities. It has little or no effect on the chronic productive tuberculosis which spreads as it pleases in the collapsed lung.

## ENDOBONCHIAL OR TRACHEOBONCHIAL TUBERCULOSIS

BENJAMIN GOLDBERG

This involvement of the tracheobronchial tract was definitely described just 100<sup>56, 57</sup> years ago. However, very little attention has been paid to its clinical manifestations until the last decade.<sup>58</sup>

Pathologically the lesions are usually found located on the postero-lateral walls of the bronchi or trachea. Available evidence and personal observation seem to point to the pathogenesis of bronchial tuberculosis, occurring from the following sources:

1. Peribronchial invasion through tuberculous lymph nodes, by paranodal inflammation, adhesion to bronchial structure and penetration of the bronchial wall or more rarely through the lymph vessels. A pulmonary parenchymal invasion by bronchogenic spread from the endobronchial lesion may then be secondary to this.

2. Endobronchial lesions secondary to parenchymal lesions may occur either by direct implantation as a surface lesion or through the peribronchial structures usually by the lymphatics as mentioned above.

3. Direct hematogenous implantation is rare.

4. The lesion occasionally may be a terminal or agonal one due to the moribund state of the individual.

The lesions vary from solitary microscopic tubercles, followed by ulcers which may invade the submucosa leaving bridges of mucosa overlying, to distinct ulcers with secondary granulations causing partial or complete obstruction of the bronchial lumen. The ulcers may become annular, and involve the entire circumference of the bronchus. In instances, cicatrization follows ulceration with cicatricial stenotic lesions causing partial to almost complete obstruction. Hyperplasia without ulceration is also not uncommon.

### Symptoms and Physical Findings.

1. A positive sputum which recurs, in the absence of a pulmonary parenchymal lesion, or in the presence of a parenchymal lesion which shows adequate healing so as to preclude the possibility of tubercle bacilli coming from it or in the presence of a parenchymal lesion, with or without cavitation, which has had a total collapse by means of artificial pneumothorax, all of which have been checked roentgenographically, is the most important consideration to direct attention to this condition.

2. Obstructive breathing, both inspiratory or expiratory, sibilant and sonorous rales or rhonchi, found in the parasternal regions, usually localized between the 1st and 4th ribs, although it may be audible standing close to the patients. Typical asthmatic paroxysms of breathing may also occur.

3. Fever may be absent in the localized endobronchial lesions. It is, however, usually low grade or may suddenly become elevated to 101° F.-103° F., due to absorption following bronchial obstruction from thick, tenacious mucus plugging a narrowed bronchial lumen.

4. Intermittent dyspnea with cyanosis at times, associated with bronchial obstruction which is usually temporary, and which obstruction causes atelectasis varying in extent based on the bronchus involved.

**Roentgen Findings.**—Uncomplicated endobronchial tuberculosis may show no definite findings on the flat or stereo film of the chest. Tracheal or bronchial obstruction only rarely is evident without the use of an opaque substance—Lipiodol or Brominal.

Atelectasis which is intermittent in its appearance is a most important finding, and of course should be followed by serial films to determine its clearance with opening of the bronchial lumen when due to sputum.

**Bronchoscopy.**—This determines the type and location of the lesions and allows of better placement of the opaque substance for roentgen films, which may more definitely outline the extent of the lesion.

Smears of the exudate on the surface of the lesion to aid in diagnosis may be taken. Biopsy is obviously not recommended.

**Prognosis.**—The prognosis is not very good. The spread of infection and reinfection bronchogenically to the parenchyma usually results in serious parenchymal lesions. Tracheal bronchial stenosis with bronchial obstruction may portend a fatal outcome.

**Treatment.**—The most important consideration is careful adherence to the usual therapeutic tuberculosis regime. Bronchoscopic aspiration of thick tenacious mucus which has caused a temporary bronchial occlusion and atelectasis, may be practiced. Topical application of epinephrine, 1:1000, or cocaine, ten per cent, may allow temporary shrinkage in the presence of edema.

The utilization of silver nitrate in solution of 10 to 30 per cent applied topically through a bronchoscope in the forms where the hyperplastic type predominates or where the ulcerative type is not completely annular.

Electrocautery has been used in some localized lesions with success. Roentgen therapy may be of value in some patients—again—where the annular type circumventing the bronchus is not present, because of stimulation to scar tissue formation and obstruction. Dilatation of stenotic lesions with fine bougies has been practiced but there is danger of rapid spread into the parenchyma and possible miliary tuberculosis where mucosal infiltration or ulceration exists.

Collapse therapy. We have tried artificial pneumothorax when it could be performed, not as a curative measure, but in the hope of preventing parenchymal spread and disease. Tracheotomy has been necessary in the presence of acute edema as an emergency measure.

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## CHAPTER X.

# X-RAY FINDINGS IN ADULT PULMONARY TUBERCULOSIS.\*

HOLLIS E. POTTER

### INTRODUCTION.

Jaffé in the chapter on Pathology introduces his subject thus: "When tubercle bacilli gain entrance into a suitable host they produce alterative, exudative and proliferative changes the extent and intensity of which depends upon the resistance of the host and upon the number and virulence of the bacilli."

If absolutely perfect the roentgen method could do no more than bring to the eye the nature and extent of the multiform lesions of pulmonary tuberculosis and show by their physical characters the degree to which their growth was being resisted or conquered by the tissues of the host.

The roentgen method is not perfect. Its records are fundamentally dependent on tissue outlines and relative tissue densities. Caseation, the most significant tissue change, may for a time be obscured by overlap when lying in the center of massive exudation, massive atelectasis or massive fibrosis even in this day of approximate technical perfection.

In the following pages I will attempt to review the points of diagnostic strength and weakness of the x-ray method as applied to adult pulmonary tuberculosis, calling attention to some of the pitfalls which lie in the path of every worker. Roentgenology is indeed a study of pathology in the living person as interpreted through the basic laws of tissue radiability.

(1) *Physical Structure of Chest Highly Favorable for Detection of Small Pulmonary Consolidations.*—More than any other portion of the body, the lungs present a physical structure in which small soft tissue changes may be visualized by the x-ray method. This fortunate situation is made possible by the large native content of air which fills all alveolar spaces and bronchi in health. It is unnecessary to recall the delicate thin walled texture of the inflated alveolus or the fact that air presents a density of only 1 to 800 as compared with water. It is well known that one and another soft tissue in the body has much the same density as water, with the major exception of fat the density of which is about 0.8 that of water.

The opacity to x-rays of the normal inflated lungs is almost negligible and its framework is very light. If it were not for the arteries, veins and lymphatics the lung fields would show almost no "veining" on roentgen films. But the lungs are surrounded by a chest wall of appreciable opacity not only in the soft tissue complex but in the bony structures of ribs and shoulder girdle. Certain alveolar

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\* The illustrations for this chapter can be read separately from the text. Each is intended to give a running account of the subject. Ed.

areas are covered by the heart; the diaphragmatic dome rises definitely higher in front to conceal alveolar areas behind it.

The relatively thin thoracic walls plus the highly translucent lungs present a complex that is indeed highly penetrable to x-rays and extremely favorable for the detection of small deposits in the lungs. Physically the deposit is comparable to the substitution of water for air in an area surrounded by air, the whole situated in a thin-walled hollow shell. From experimental and autopsy data it has been determined that an average lung consolidation the size of a pea and

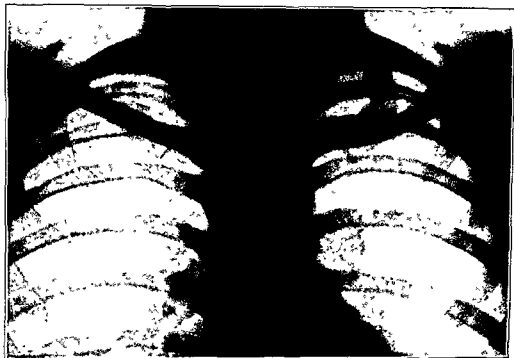


Fig 1—Left apical involvement. A general haziness in left apex may be analyzed into a multiplicity of small nodular infiltrations rather discrete and each presumably representing a tuberculous colony plus a very limited perifocal exudate. The lack of general exudate extending in a widespread manner over the involved apex argues toward an early tendency to heal and shows absence of unusual allergic reaction in the individual.

of the density of water when surrounded by air-filled lung is easily demonstrable by x-rays and it is everyday experience to see pulmonary lesions much smaller than this.

Recent experiments wherein a hollow box with metallic walls approximating in x-ray opacity that of the thorax was made to contain at various locations a small piece of cardboard 4 mm. in thickness which by test approximated the x-ray opacity of tuberculous lung tissue. This "equivalent" was found to be easily visualized on films made by ordinary chest technic. Other experiments showed that it only became undermonstrable as the depth of air in the hollow container was greatly reduced so that the "equivalent" was robbed of its high air density-contrast.

In practical work films are usually made by rays emerging anteriorly. In this projection the shoulder blades may be rounded forward to throw their shadows clear of the lungs and the divergence of the rays is favorable for including much of the pulmonary tissue which lies behind the diaphragm. For the lowest post-diaphragmatic areas an oblique or lateral view may be required.

To displace the minor lesions with reference to the ribs and to localize or orient overlapping pathologic structures two separate films made in vertical shift are advisable. They may as well be made in stereoscopic shift and read stereo-



Fig 2—Left apex and subapical region clouded by homogeneous exudate with only the hint of an internal pattern. Typical in location for primary reinfection. The predominance of exudate drowns out nodular foci which might have been visible otherwise. On resorption of the exudate residual areas of involvement may be predicted. Only in the most allergic individual will such an exudate be found to clear away completely in a short space of time.

scopically. Physical conditions, therefore, favor stereographic pairs from behind, made in vertical shift; conditions also favor fluoroscopic study for all gross changes, particularly for orienting cavities.

Many users of the x-ray method become hide-bound in their habit of always viewing stereo chest films in the stereoscope whereas others of much experience demand two films made in stereo shift, or preferably a little greater than true stereo shift, for separate viewing. An adequate test made by a number of experienced observers on a long series of films showed no essential difference in the reading for tuberculosis whether or not the stereoscope were used. The stereo method is primarily of value when lesions are multiple, complex and

superimposed. The stereoscopic view aids materially in orienting them. It is a mistake to believe that lesions not visible in two flat films will become visible by the process of stereoscopy.

Stereoscopic radiography cannot be too highly praised for "sensing" the relative depth position of foreign objects in the chest, whether opaque bodies in the bronchi, foreign materials injected for diagnosis, pathologic deposits in the

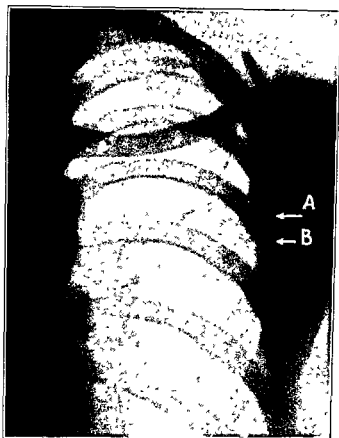


Fig. 3.—A small patch of infiltration of such pattern and location as to be immediately suggestive of tuberculosis. (A) The pattern shows limitation at borders by pulmonary septa. The central consolidation is not very dense. It is a minimal lesion. (B) Trunk markings leading to hilum are more than normally prominent. This is also true of two trunks leading higher toward the apex although the latter are not seen to terminate in any consolidated areas above. Inference: A minimal subclavicular infiltration of tuberculoid type with lymphangitis of neighboring trunk structures.

lungs or interlobar pleural exudates. Perhaps an undue emphasis has been placed on the stereographic method by some who are technically not masters of the single film. Those who never use the stereoscopic method fail to appreciate how commonly tuberculous deposits lie far posterior in the upper chest.

A fluoroscopic study before making films aids in recognizing the major lesions, aids in planning the radiographic procedures and teaches one the thickness of chest wall in the case. During this time the patient is taught to hold his breath quite still for the subsequent radiographs. By the screen one may fail

to see at all the smallest disseminated lesions, especially when they occur in a similar pattern on the two sides. Lesions in the shoulder periphery are apt to be missed in large individuals. Cavities and interlobar accumulations are easy to orient by this method.

Fluoroscopy is done by relatively "soft" rays during frequent shifts of tube and patient. By this method overlaps are appreciated even as well as in stereo-

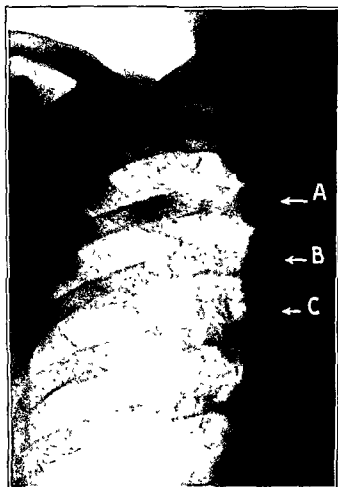


Fig. 4—(A) A more homogeneous patch of consolidation in right first interspace, a most common site for primary reinfection by tuberculosis. Calcification in peritracheal (B) and peribronchial (C) lymph glands suggest site of ancient primary infection. The uniform density of the parenchymal patch (A) classifies it as an exudative lesion. The fairly discrete margins argue that peripheral resorption has begun. No denser nodes of consolidation can be identified within the area involved.

scopy. A short period of fluoroscopic study followed by a routine pair of stereo films and supplemented when advisable by off-angle films to cover in best manner individual situations which might present confusing overlaps, is the one best routine procedure.

With present day facilities and technic roentgenography for adult lung tuberculosis has become an invaluable adjunct to the clinical examination. It

has become orthodox to the extent that the internist or specialist who ignores its value is rapidly passing. Should there have been no other purpose accomplished in the development of roentgenology than the service rendered in chest diagnosis that development would have been justified.

(2) **The Hilum and Trunk Markings of the Lung; the Bronchial Tree**

—The emphatic statements which were just made regarding the physical structure



Fig. 5—Multiple small foci produce a stippled or granular appearance in right sub-apical region. Such infiltrations may be expected to heal without production of much linear or nodular scar. See next illustration.

of the alveolar areas of the lung, which makes the demonstration of small tuberculous infiltrations possible, do not pertain to the structures at the hilum. On the contrary the physical conditions are so much different that significant disease may at any time be present in the lymph glands at the hilum which can not be detected by x-rays. It is a good working rule, therefore, to emphasize x-ray values in the main lung areas and minimize the values at the hilum.

The hilum structures as seen by x-rays are found to vary so much in healthy individuals that one can scarcely define the limits of normal. The hilum is a complex of lymph nodes and converging trunks of arteries, veins and lymphatics together with the interstitial tissue which carries them. The main bronchus passes through this complex but if empty does not contribute particularly to the shadow complex. The trunk markings of the lung as seen in films are mainly

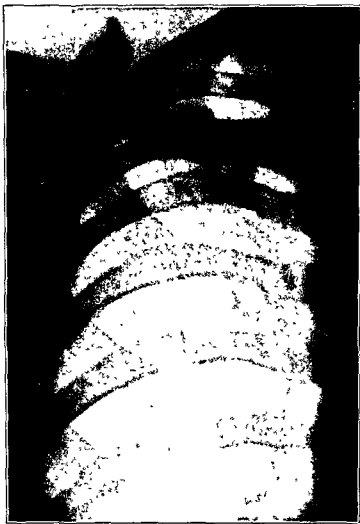


Fig. 6.—Same case as Fig. 5, three months later. One gets the impression that this is now a near-healed lesion. No nodular formations persist. Fibrosis is of small extent.

caused by the vascular and lymphatic trunks together with their interstitial tissue. The smaller bronchioles when empty are almost invisible. Lymphatic glands are mainly located about the larger bronchi. Some small glands are found further along the course of the lower main trunks than in the branches toward the upper or middle lung areas.

It has been aptly said that 85 per cent. of the shadow caused by the normal trunk structures of the lung is caused by the vascular structures and at the hilum

itself much of the shadow is due to the larger pulmonary vessels. In the general branching and rebranching of the bronchi as they approach the periphery the general architecture of the lung is such that the veins, the arteries and the lymphatic branches tend to travel close together.

Of these branching structures which produce the veining of the lungs in roentgen films, the lymphatic channels are perhaps the most interesting from



Fig. 7—Widespread nodular infiltrations of nearly all of right upper lobe. The peripheral lesions show exudative characters. The predominating appearance suggests favorable resorption between nodules. Possible caseation in limited area below clavicle. Cavity not predicted. Lesions largely of a "productive" type.

the standpoint of tuberculosis just as at the hilum the lymphatic glands are the most important. Tuberculous involvement of the tracheobronchial lymph glands is common. It may be present in cases where there is a frank tuberculosis of the lungs but in adults it should be considered quite separately. In the peribronchial lymph glands tubercles may live and grow and heal and calcify without producing more recognizable change in x-ray films than is caused by the calci-



fication itself. The physical structures here are such that with the variations in the hilum picture in various healthy individuals the x-ray inferences are limited to a gross homogeneous enlargement of the gland or to the accidental calcification later on. Massive uniform enlargements of the peribronchial lymph glands in adults are not common and when present their identification as

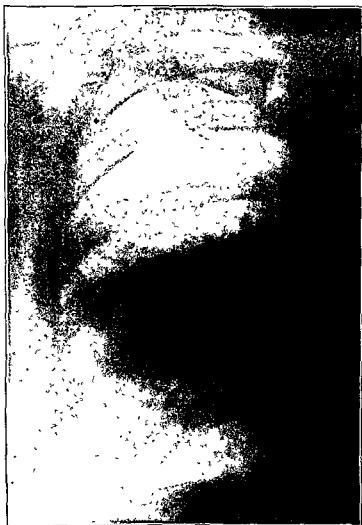


Fig. 8.—The right middle lobe shows a massive exudative involvement, not sufficiently dense or well marked off to indicate complete serous exudate in peripheral portions of the lobe. No internal markings disclose a pathologic pattern within the area. In this type and stage of involvement the x-ray findings are quite such as one expects in simple pneumonia.

tuberculous will depend rather more on a clinical study than on any characteristic x-ray appearance. They must be differentiated from all other conditions which may give such glandular enlargements either primary or secondary.

The reason why a small tuberculous focus in a lymph gland is not as visible to x-rays as a tuberculous focus surrounded by air is, of course, because of the lack of the air contrast within the gland. The air of the lung only helps to

show at margin the gross enlargement of the gland itself and in a diffusely enlarged tuberculous gland there is no internal pattern shown to suggest its tuberculous character. Calcified nodules in peribronchial and peritracheal lymph glands are usually thought to indicate previous tuberculous disease. However, most pathologists insist that fibrosis is the terminal stage of healing and that calcareous replacement is a common, but not an essential accident. As such the

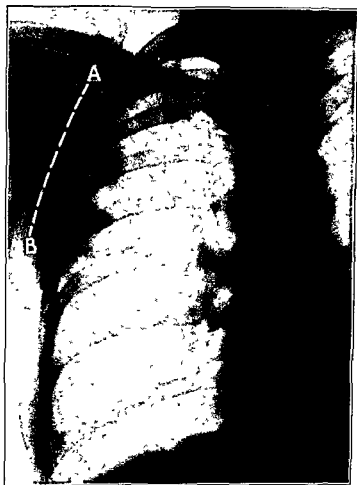


Fig 9.—Almost complete clearing of massive exudative involvement of right upper lobe. Only a vague homogeneous semi-opacity is seen at the shoulder periphery (*a-b*) where lymph drainage is toward pleuræ. No mottled or nodular formations of any size are visible in the cleared areas. One may predict a favorable outcome and may reasonably doubt the diagnosis of tuberculosis unless bacilli are found.

calcifications are not specific for tuberculosis and might be found after the healing of other infections.

When pulmonary infiltrations of tuberculous type are present at lung peripheries and one sees also an increased width and density of the trunk markings which lead from this area to the hilum and perhaps in addition some increase in the hilum itself one may be justified in the interpretation of tuberculosis in the peripheral areas and of a suspicion of tuberculosis in the regional

peribronchial lymph gland. One is practically never justified in making interpretation of tuberculosis in the trunk structures which connect these two areas. The increased visibility of trunk structures is commonly caused by an infiltration along the lymphatic channels and is referred to as a lymphangiatic reaction. Concerning these values and concerning the question of whether the disease is

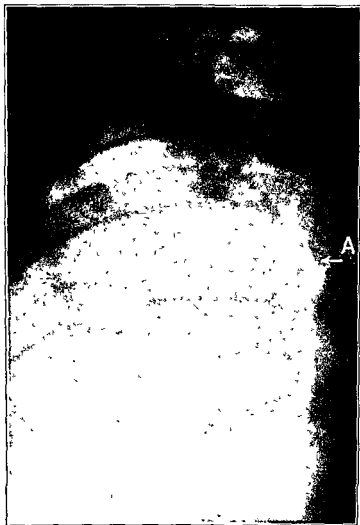


Fig. 10.—Partial clearing after massive exudative stage in right upper lobe tuberculosis. The clearing is advanced to a stage where some caseation may well be inferred. At level (*A*) a thin walled cavity is probably present. Other areas look rather too mottled to encourage expectations of complete and rapid resolution. Some interstitial fibrosis is suggested in areas leading to the hilum.

primary at the hilum or periphery, there has been much argument both in the adult and in the childhood form of tuberculosis. From the standpoint of adult pulmonary tuberculosis it is my opinion that mistakes will be largely avoided if no inferences are made as to tuberculosis in the trunk structures, and but simple suggestions made as to the possible tuberculous nature of enlarged hilum glands. But with respect to tuberculosis in the pulmonary areas the value of

x-rays can hardly be over-emphasized both as to its presence and as to its probable nature.

(3) **X-ray Character of the Earliest Demonstrable Lesions.**—Wm. Snow Miller and others have described the tiny tubercle as it first gains foothold in the parenchyma of the lung. This original lesion of microscopic size has no



Fig 11—Advanced clearing after widespread involvement in right upper lobe. Some caseation has probably occurred at zone (A) below clavicle but the lack of conglomerate islands and the tendency to a linear network in this area argues strongly that complete fibrosis may be anticipated.

physical characters which would make it demonstrable by x-rays. Its first visibility is made possible not by the tuberculous colony itself but by the stimulation of a regional exudate or collateral inflammation which is of about the density of water or blood and as such is greatly in contrast to the density of the air-containing lung which surrounds it. It is occasionally our privilege to see single or multiple patches of infiltration of very small size which by their character and location suggest a very early invasion by tuberculosis and which

followed through the months have proven to be so. Such lesions are most commonly brought to light in the x-ray room during a routine study or in contact cases under examination because of a tuberculous death in the family. Occasionally a very small lesion is brought to light because of hemorrhage which may be an early accident. Seldom are such tiny areas disclosed as the single change



Fig. 12.—Here a caseous pneumonic involvement of right upper lobe has left some irregular areas which are rather too ragged in appearance to indicate a promptly favorable result. All through the apex and below the clavicle are islands of residual density any one of which might be the residual focus for a reinfection.

in cases coming to the clinician because of local or general symptoms. Occasionally they are found as the only change in the lung after spontaneous pneumothorax.

The earliest demonstrable lesions have been observed in at least three types. The first type has a simple diffuse homogeneous shadow density that can not be differentiated from a nontuberculous bronchopneumonic patch and has the uniform opacity of edematous lung. It is likely to be triangular or conical in shape,

conforming to the lobular construction of the lung. The interlobular septa lie at the limits of affected areas and act as barriers to regional exudation. The total area of exudation may be small or large in relation to the actual tuberculous focus, depending upon the allergic reaction of the individual. The tuberculous character of the simple exudative lesion must often remain in doubt until resorption of the exudate reveals the underlying focus.



Fig 13.—Partial resorption in exudative type involvement of right upper lobe. The irregularity in clearing suggests many small but no large areas of caseation. No signs of cavitation. One may predict a nearly complete resolution with mixed nodular and linear fibrosis.

A second type is a single blotchy area more or less conical in shape, perhaps with lobulated margin and irregular pattern within. It may look exactly like the larger patches of exudative productive tuberculosis with which we are familiar but simply miniature in size.

In the third type a given area of the lung is the seat of numerous tiny consolidations each poorly outlined and not larger than a grain of wheat but altogether producing a granular or flocculent appearance. The intervening alveolar spaces do not as yet appear to be the seat of collateral inflammation. In such a case it is probable that a shower of tubercle bacilli entering a given

bronchus split into numerous small doses and develop a large number of tiny tuberculous foci simultaneously.

The location of these earliest demonstrable lesions is important. They are most commonly found in the upper lung fields at the periphery which lies just below the clavicle. Their second most common site is in the apex itself. Less commonly they are found down as low as the second rib but in the adult form



Fig. 14—Left upper involvement with fibroid changes predominating. No large caseous areas. No signs of cavity. The disease has always been of benign type, slowly progressing, and showing great tendency to heal. Such involvements are often insidious in onset and perhaps discovered by accident.

they are usually above the level of the hilum. When occurring in the apices of lower lobes they are commonly seen high in the lung but at the periphery toward the mediastinum where they may be easily overlooked. Stereoscopically and at autopsy they are seen to occupy, as a rule, the posterior areas of the lung rather than the anterior.

In the first and third types there are usually no signs of increase in the trunk markings which lead from this area to the hilum. In the second type an

increase in trunk markings may develop early. An increase in the size of a hilum gland to which this increased trunk leads is presumptive evidence of a secondary glandular reaction whether or not the gland is infected by tuberculosis.

Exactly the same three types of early tuberculous involvement are to be found in cases of frank tuberculosis of the lung when dissemination has occurred to a distant portion. It is somewhat from a study of such areas of reinfection that one gains confidence in identifying the reaction of minimal tuberculosis when it occurs as the first and only pulmonary change.



Fig. 15—A widespread exudative process in right upper lobe giving a general watery cloudiness through which one may vaguely perceive some large nodular islands of greater density. With the resorption of exudate one may expect a persistence of these islands as caseous nodes. No signs of cavitation are apparent. It is too early to rule out the possibility of small cavities developing at caseous areas.

It is, of course, not expected that such minimal findings will be disclosed in patients first applying to clinicians on account of pulmonary or general symptoms. Their discovery by x-rays is of more than academic interest and their true significance may only be determined by a further series of clinical and roentgen observations made from time to time in succeeding months.

In the massive consolidations of pneumonic or bronchopneumonic type which occur in tuberculosis with acute onset the x-ray method is of great value in showing the presence and general extent of involvement but its tuberculous pathologic character may be quite obscure until partial clearing of the exudate has taken place.

(4) **Advance of Disease by Extension and Reinfection; Miliary Dissemination.**—Roentgenography and roentgenoscopy furnish valuable information



as to the pathologic course of the disease after discovery. In lesions of the exudative type pronounced changes may occasionally be seen in a few days time whereas in the more chronic form involving considerable fibrosis very little change may be observable over a period of two to six months. The rapid fluctuations which are sometimes observable in connection with exudative lesions are often not as important as changes in the lesions having a definite pattern although a permanent resorption of exudate is favorable. Changes which represent a real organized healing or on the other hand a real spread of the disease are highly valuable.



Fig 16—Large dense area of caseation remains in upper left after partial resorption at periphery. Caseo-pneumonic character amplified by central area of clearing suspicious of cavity (*A*). One may predict a further resolution and fibrosis for other areas.

It is commonly observed that an extension of the process occurs within the same lobe. New consolidations develop in adjacent lobules by direct extension, but much more often by reinfection through the bronchial route. The original focus and, indeed, all further extensions depend considerably on whether a large number of bacilli gain foothold in a given area or whether small numbers begin simultaneous growth at a number of different points. Multiple areas increasing in size and overlapping each other may merge and overlap to the formation of irregular conglomerations. If there is not too much collateral inflammation the lung field will still give the "mottled" effect. Not infrequently this process continues until the tissue of an entire lobe is involved.

Spread by autogenous reinfection may at any time be brought to light in other lobes. The most common partners in a double infection are the upper lobes which seem most vulnerable in adult tuberculosis. Often one sees both upper

lung areas almost similarly involved down to a given level. More often the involvement is unequal and one may usually recognize by the difference in type or age of certain lesions that side which was the seat of the original focus.

Again, a spread of the disease may occur as a cross infection to other parts than the apex. It is a rather frequent picture to see the right upper lobe considerably affected and to see a few small patches in the mid lung region at left axillary periphery. Spread to the bases is often recognized in patches which more resemble bronchopneumonic consolidations than those visible in the upper fields. They may lack the mottled "tuberculoid" appearance.



Fig 17.—An old right apical involvement has largely cleared but has left a definite island of consolidation giving the appearance of a cascated node. This was unchanged at six months' intervals for five years at the end of which it was seen to have broken down and the whole apex and sub-apical region were studded with small nodules indicating a reinfection.

All such reinfections are of the general nature of metastasis and commonly take place by spilling through the open bronchi. They can hardly be distinguished by x-rays from the exogenous reinfections which sometimes develop independently in an area where an old process has been rather well healed out.

The rapid and widespread dissemination which sometimes occurs whether through the bronchi or through the blood stream and known as miliary tuberculosis is more in the nature of an accident and merits separate classification.

(5) **X-ray Evidences of Activity; Chronicity; Healing.**—Any collection of x-ray films showing adult pulmonary tuberculosis portray lesions which differ widely in their physical shadow-appearance. Their outline forms, their structural patterns and their density differences furnish material upon which valuable

inferences as to the "present activity" and the "tendency to heal" may properly be based.

In a new case where the diagnosis is first being established the x-ray not only furnishes invaluable confirmatory data, but to the experienced observer it may present equally valuable information as to how the invading disease is being resisted by the body tissues. Such information aids in classifying the patient for prognosis and treatment. A "tendency to heal" before the stage of gross caseation is reached carries with it an entirely different outlook than when the



Fig 18—Partial resorption after an exudative involvement of right upper lobe. The irregular clearing reveals suspicious round area suggesting cavity below the clavicle. Peripheral absorption incomplete. Evidence of beginning fibrosis in trunk structures. It is important to note that this is not a simple sub-clavicular infiltration but a caseous pneumonic involvement with probable cavity.

individual is unable to resist the onslaught and a trend toward caseation—cavitation—ulceration is established.

Likewise, in the further course of the disease when reinfections occur, similar observations of value may be made as to whether the trend is toward caseation or whether this stage is resisted or aborted.

X-ray rules governing the appearance of active lesions may be stated as generalizations, but should be somewhat modified in their application to the various lesion-types already mentioned in Section 3 on "the character of the earliest demonstrable lesions" and further to be discussed in Section 10 which relates to "classification according to predominant lesions present."

Applying conceptions of activity to infections or reinfections which at first from an x-ray standpoint are purely exudative in character, and mentioning this

class first because of logical sequence rather than because of its importance or frequency, we find that the apparently simple exudate of lobular, lobar or other size may or may not be later found to have obscured by its unusual amount of collateral inflammation the lesions of tuberculosis having an organized pattern. Two general situations must be considered. First, there may have been an unusually pronounced amount of simple fluid material collected in a widespread area about a relatively small focus of disease in an especially allergic individual. In this case the exudate clears away in a short time and clears away completely so

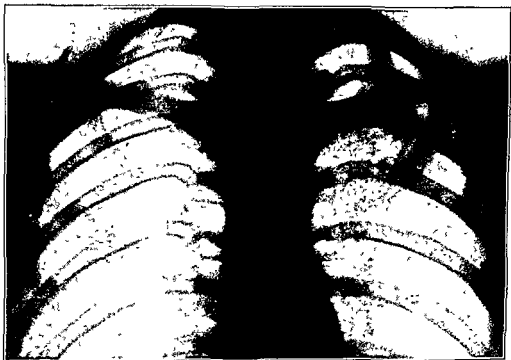


Fig. 19—Localized left subclavicular "fan" with partial resorption, some residual exudative manifestation toward periphery and converging linear structures of increased prominence. Having passed the peak of activity one may predict a favorable result. Patches of irregular resorption must not be confused with cavity in this case.

that from an x-ray standpoint it was simply a pneumonia or bronchopneumonia. Its tuberculous character is suspected by the absence of certain clinical criteria of pneumonia or perhaps proven by the occasional finding of the organisms. The uncharacteristic x-ray findings in this condition may be freely confessed.

In a second set of cases where x-rays show only the exudative signs of simple pneumonic consolidation a large dose of bacteria have gained simultaneous foothold in a lobe (usually an upper); the patient is sicker; there is no crisis and the consolidation persists. From this point on it may progress as in acute pneumonic phthisis or areas of clearing may develop as in more benign caseous-pneumonic tuberculosis. In the latter instance, a correct interpretation of the process of clearing is very important. Irregular resorption with the persistence of conglomerate areas of consolidation comes to mean caseation. Clearing

between the islands is, of course, favorable as indicating the first stage toward healing. The development of more or less central ragged areas of translucency within the lobe consolidated or within the denser islands may indicate sloughing of caseous material and formation of cavity.

We pass now from that rare form of activity represented on the roentgen film on first discovery as a simple exudative pneumonic consolidation to the much more common condition where the active consolidations are nodular or patchy in form and surrounded by air to such an extent that their physical characters



Fig 20—The entire left upper lung has been the seat of active caseopneumonic disease but now shows pronounced scar formation at points not the seat of cavitation. Two cavities are quite obvious near shoulder periphery. They seem empty but are likely responsible for the cross-infection seen beneath right clavicle. Here scattered nodules evidence a recent spread of the disease.

are better shown. In general such lesions lack density and answer well to the terms "finely nodular," "flaky," "stippled" or even "granular." At margin they may show a "melted" or watery appearance caused by a thin zone of exudate or "collateral inflammation." In fact the main shadow of a minor lesion is cast by the perifocal deposit rather than by the tuberculous process itself.

Such changes will show well only on films that possess the proper balance between detail and contrast. They will be "burned out" in films over-exposed by deeply penetrating rays.

The more or less discrete lesions not accompanied by a gross exudative response may well be spoken of as "productive" or "proliferative" in type in that they soon show under favorable conditions more discreteness because of resorption of regional exudate and perhaps an admixture of a linear pattern

caused by lymphatic reaction and beginning fibrosis in the septal and main trunk structures. Under more favorable circumstances the little nodular foci shrink in size and fade out entirely so that in a year or two the lung area looks normal or shows at most a simple accentuation of the neighborhood trunk markings.

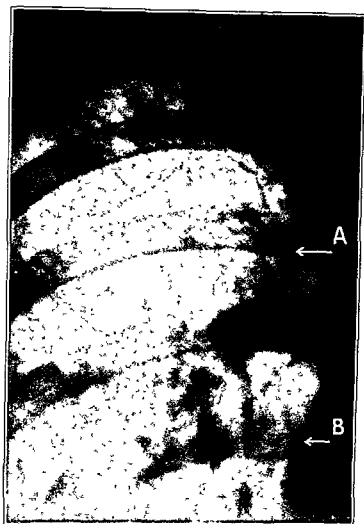


Fig 21—The importance of serial films made at intervals depending upon the chronicity of involvement and varied by any change in the clinical complex must be acknowledged even in widespread tuberculosis. Experience teaches one to recognize the favorable appearance at (A), where perilobular fibrosis and lobular emphysema predominate. One views with dread the newer developments at level (B), where lesions show more exudative characters. The larger lesions will be watched for signs of productive scar on the one hand and the consequences of caseation on the other.

Should, however, the pathologic process have advanced to the stage of caseation before resorption began there will be left for a long time a rounded or oval node rather homogeneous in density which resists the processes of resorption and fibrosis apparent with respect to the non-caseated lesions. Such a caseous node lying quiescent and apparently encapsulated must be considered a menace

because of the probability of a breakdown and further reinfection. The writer has seen several such instances after a quiescence of some years.

The favorable resolution of the caseated focus involves the discharge of caseated material through the bronchus, or a shrinkage in size and replacement



Fig. 22.—A mid-lung field section shows many lesions of simple exudative character but denser areas at levels (A) require classification of caseopneumonic disease. The translucent areas at (B) and (B) have no characters of fixed cavity but will be viewed with anxiety till further regional clearing occurs. Further areas of reinfection would be no surprise. The beginnings of fibrosis cannot be recognized at any point.

by fibrous tissue. A secondary replacement by calcareous material is often the end result in the smaller lesions.

Evidences of activity, chronicity and healing are more difficult to detect and evaluate in cases of chronic ulcerative tuberculosis where there has been massive caseation and cavitation in lesions of various ages and when additionally there are present in superimposed or adjacent areas the newer lesions of more recent

reinfection. In such cases extensive areas of fibrous tissue may be recognized as such or confused with an attendant atelectasis. General density of lesions argue well for a healing process, but some caseated areas not yet cleared by the sloughing process may be entirely overlooked. It might be said, in general, that



Fig 23.—The character of predominating lesions in this left upper lung is entirely toward the fibroid type. The stringy appearance throughout evidences a former involvement that has resolved except for semidiscrete scar. The spongy appearance at level (A) must have resulted from slight cavitation but no ring-shaped cavities are visible and one may predict that none will result.

where extensive caseation has taken place the fact of extensive fibrosis is favorable but that no x-ray inference of complete healing is justified.

The extreme of fibrosis in proportion to active areas is often visible in fibroid phthisis. At any given period the whole picture may be that of linear and nodular scar with only here and there a lesion of the active type and none showing extensive caseation.



(6) **Evidences of Caseation; Cavitation; Ulceration.**—When a given area of lung tissue is attacked by a large number of tubercle bacilli at once, there is a rapid exudation in the whole area surrounding it and inasmuch as the lung tissue is overwhelmed by the virulence of the attack the central portion succumbs and caseation follows. This area of tissue death may be large, small or multiple,



Fig. 24.—Here the picture is quite different. Exudative and caseous lesions occupy the entire mid-lung area. These have become established by widespread reinfection from right apical cavity in a case which otherwise would not have been classified as far advanced. Serial films can hardly be expected to show a favorable trend toward healing.

but before healing can occur the caseous material must undergo liquefaction and discharge. This leaves an empty space with ragged or smooth walls which may or may not become healed by the simple process of productive fibrosis. Should the unfavorable result occur and a persistent cavity develop then is one faced with one of the most difficult problems of tuberculosis therapy, and the prognosis is immediately modified. Because the first stage x-ray appearance is that of

simple pneumonia or bronchopneumonia its differentiation as tuberculosis is difficult even when elsewhere in the chest one may recognize lesions of a tuberculous character. However, it runs a different clinical course than pneumonia, failing to culminate in a crisis. During the process of resorption in the second stage one may detect the first x-ray signs of caseation. As a rule resorption is not uniform throughout the consolidated area and when decidedly patchy it is reasonable to suspect that the resistant areas are the seat of caseation. A further clearing may, however, take place, and then only the islands of true caseation

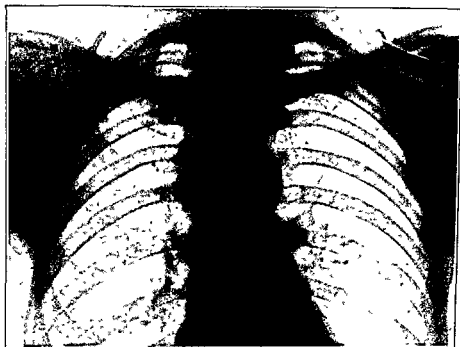


Fig. 25—With bacilli found in sputum the only roentgen findings were along paravertebral border above right hilum. The changes are rather limited in extent but definite. Their location is proper for the apex of lower lobe. Stereoscopy shows a posterior position. The "paravertebral" form is placed in a special classification from "subclavicular," etc. Patchy infiltrations must be present; not merely exaggerated trunk markings, to justify the inference of significant disease.

are set off by contrast with the intervening areas of normal or emphysematous lung.

In those cases where a massive area of caseation develops the fact may first be recognized when a central area is evacuated of its caseous and liquefied material. A cavity may be recognized as an irregular space with ragged edges. It may be that peripheral portions of the lobe clear very slowly or not at all. The caseating process has interfered with lymphatic drainage. The appearance of consolidation persists; first, because of unabsorbed exudate and later because of atelectasis and fibrosis.

Small and favorably drained cavities may collapse and heal completely. The negative pressure and shrinking tissue about them often prevents this, however,

and the fact that they are connected with a bronchus favors their persistence, their inflation to a rounded form, and the development of a reservoir of infective material which may spill upon occasion to other portions of the lung throughout the patient's life. Much has been learned in recent years concerning the life history of various types of cavity, particularly as to the mechanism by which certain cavities may fluctuate in size or even rapidly disappear, depending on the efficiency of certain tissue formations within the bronchus acting as valves with respect to entrapped air and fluids.



Fig. 26.—Mainly a left sided tuberculosis with most lesions centering about left hilum. A prominent cavity is seen at first interspace and one less pronounced lies near hilum structures. These cavities together with spread of disease already present are in themselves criteria which justify a very guarded prognosis. Further breakdown by caseation may be predicted.

When serial x-rays during the stages of resorption show islands of persisting caseation it may be true that these can never be recognized as the seat of cavitation, especially when they are of lobular or acinous size. They may seem to gradually shrink in size and persist as small hard discrete nodules, eventually, perhaps, becoming calcareous. There is often seen a caseous node which neither shows signs of evacuation nor fibrosis. For a long time it may remain quiescent without marginal or internal changes that can be detected. Such caseated islands in a resting stage must not be discounted as innocent encapsulated terminations of disease without further danger, for they may be seen to break down after years of quiescence and furnish infective material for a widespread reinfection.

Cavities tend to take on a rounded or oval form. More or less granulation and fibrous tissue gives them a thin or thick wall. They may ulcerate and progress in size, perhaps coalescing with others adjacent. In certain cases they

appear to be entirely cut off from regional bronchi and fail to function as expected from the descriptions in the older textbooks. The x-ray method has been severely criticized in appearing to show cavity when it could not be confirmed by physical diagnosis in persons not raising material as from a cavity. On the other hand autopsies show ragged cavities in the midst of caseated lung areas which can not be interpreted with confidence in ante-mortem x-ray films. The impression today among careful workers is that x-rays are an indispensable



Fig 27—(See also Fig 28.) A rather massive tuberculous involvement in right upper lobe has resulted in caseation and cavitation, the rather large cavity centering at clavicle. All other lobes were negative at this time. The dangers of the open cavity were minimized by the patient after a pick-up in general symptoms. Patient refused most urgent advice to submit herself to sanitarium treatment.

aid in recognizing well established cavities and that ring formations in tuberculous areas can not be brushed aside as meaningless when clinical confirmation is lacking.

The location of cavities in the lung has been studied from stereoscopic films in 204 cases presenting 268 cavities by Sweany, Cook and Kegerris. About 98 per cent. are found to be located in the posterior upper peripheries and evidently in relation to bronchial branches which are directed sharply backward. It is suggested that this angulation prevents free clearance of products after caseation and liquefaction. See their drawing in Fig. 33.

They summarize their observations thus: "The pertinent facts in this work show that the great percentage of primary-reinfection cavities are located in very definite localities of the lung. In fact, certain regions seem to be vulnerable to early reinfection, perhaps corresponding to definite bronchi. The most common

region involved is that corresponding to the posterior subapical rami of the upper-lobe bronchi. The next in order is the horizontal ramus on the right and the apical on the left, all of which seem to be the most posterior branches. This posterior aspect is equally applicable, if not more so, to early reinfections than the term *infraclavicular*. Judging by this work and pathological observations, we feel that there is no one factor as important as the posterior position. 'Infraclavicular' is rather loosely understood to mean the region in the second,



Fig. 28—(See Fig. 27) Nine months later one sees an increase in size of cavity in right upper, further extension of involvement on right side and a widespread cross-infection involving the upper half of left lung. The "spill" from the cavity and "seeding" of other lung areas was undoubtedly accelerated by gymnastics carried on at the advice of a friend to "build up her body and make her hard." The "friend" was a teacher in calisthenics. One intervening pair of films showed cavity extending only half way up the apex. At that time there were still no lesions showing on left side.

third and fourth interspaces, while a large number occur in the apices of the lower lobes corresponding to the fifth, sixth and seventh interspaces, which correspond to the first posterior branch of the lower-lobe bronchus. How prophetic was Fowler's description, when he stated that the lesion is most often found 'an inch and one-half below the summit of the lung, and rather nearer to its posterior and external borders. A second and less usual site of the primary affection of the apex corresponds to the chest within the first and second interspaces below the outer third of the clavicle.' "

Such diagrams as are shown in Fig. 33 are useful by themselves in showing the common sites of primary reinfection in caseous-pneumonic tuberculosis inasmuch as cavities tend to form at the center of maximum tissue destruction.

(7) **Evidences of Arrest; the Near-Healed Stage; Healed Tuberculosis.**—When lesions can be recognized as having reached one of the further stages of linear or nodular fibrosis and when this appearance of healing has persisted for six months or a year without reactivation one is justified in the inference that the disease is "arrested." Many observers believe that proper roentgenograms furnish a better basis for the conclusion than any other criteria. While any sort of active lesions remain, however, the lack of progressive development must not give a false sense of security for the reason that if the régime of treatment is



Fig. 29—Here is a very good example of the healing in pulmonary tuberculosis in all areas except those occupied by cavity. Particularly in upper right there has been a massive involvement with nearly complete resolution about the rim of cavity. Converging toward the hilum thick fibrous bands speak for the strong tendency to heal. Both cavities contain a small amount of free fluid.

abandoned or intercurrent infection lowers the resistance, the lesions may become altered and again show roentgen signs of increased activity and extension.

The word "arrest" therefore must be used with considerable caution. Various clinicians hesitate to apply it in any cases where x-rays show the least suspicion of activity, but reserve it for those which have actually developed the major signs of healing. These signs must also have persisted over a long series of months with never a sign of reactivation or reinfection.

As all the signs of exudation disappear and the remaining changes consist of discrete nodules, exaggerated trunk markings, and some additional network of linear scars with all intervening lung spaces clear and no signs of moisture; and when these appearances persist for a year or more without ever a sign of new disease, one is justified in assuming that many of the lesions are healed and most of them are so nearly healed that a complete recovery is not only possible

but may be well hoped for. The fear of possible exacerbations may continue for years, however, and one is entirely justified in refusing to assume from x-ray evidence that a complete and final healing has occurred, particularly in cases where caseation was present, until the lesions have only the ear marks of complete healing. Until they have stood the test of time it is safer to call them "near-healed."

Completely healed tuberculosis leaves markings on the x-ray film almost in proportion to the stage of destruction that was reached at the height of its

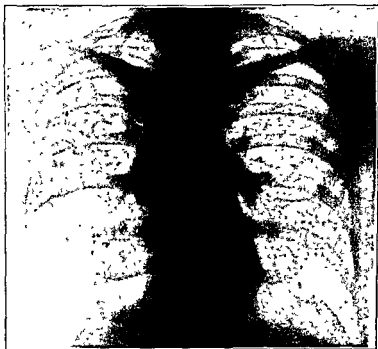


Fig. 30—A widespread mid-lung field involvement of both sides is complicated by several large thin-walled cavities which fluctuated in size from one time to another. The parenchymal lesions are mainly small and lack the density expected in caseation. There was much systemic reaction, much sputum and finally death from hemorrhage.

activity. Where caseation has occurred much lung tissue has been destroyed and the fibrosis will be pronounced. On the other hand there can have been a considerable fan of involvement showing exudation and proliferation which may be so completely resolved that no nodular formations will be visible on healing and the trunk markings may be shrunk to an almost normal size.

Fibrosis or scar is the end result of healing. Calcification is very common in these lesions, but it is more of an accidental occurrence than a necessary sequence. Calcifications are most common after caseation, whether in the parenchymal lesions or in the lymphatic glands. Occasionally the striate structures themselves show high grade calcification on healing, but only instances where the peripheral disease was well established and involved local caseation.

It is, perhaps, easier to make inference of final healing in the lesions of the upper chest than in the bases where autogenous reinfection may have occurred

in later stages of upper lung field involvement. This results from the fact that it is more difficult to interpret the significance of widened or shaggy trunk markings which in the base are ordinarily more profuse than toward the apex and which in certain individuals have become prominent because of non-tuberculous infections in the dependent portions. Also because small tuberculous areas scattered through the lower lobes of the lung are not likely to be as typically tuberculoid or mottled in appearance, but may be seen as patchy infiltrations hardly separable from the trunk markings in the films. A few cases will be found where the

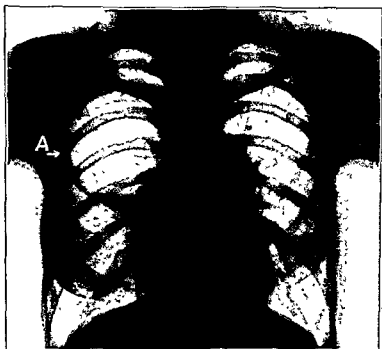


Fig. 31.—Without evidence of infiltrative disease in main lung fields the right chest shows an enormous thin-walled cavity (*A*). The delicate upper wall can hardly be made out in the anterior film. A small amount of thick fluid at dependent portion fluctuated amount from time to time. The size of the cavity can only be explained by a check-valve mechanism.

x-rays justify an inference of complete healing in the upper lung fields while still demanding a guarded inference regarding the bases. Clinical signs of exacerbation may be present after every cold and the finding of occasional tubercle bacilli may be no surprise.

Fibrotic contractures in the upper lobes are often seen to distort or displace the tracheal air column toward the affected side. This sign alone indicates a considerable degree of healing and incidentally may account for a hacking throat cough on a mechanical basis.

A massive fibrosis may occasionally be seen in association with atelectasis of regional lung tissue producing on the x-ray film a dense uniform shadow in which the two processes can not be distinguished. In combination they may serve to mask any residual areas of caseation in that field.



(8) **Importance of Serial X-ray Studies for the Early Recognition of Cavity.**—I have heretofore occasionally mentioned the advisability of making serial x-ray studies in tuberculosis in order to confirm from time to time the apparent clinical improvement or the opposite. In this manner one may get very good evidence of a tendency toward healing and can get early signs of reinfections or spread of the disease into other parts of the chest. The intervals at which these studies should be made will vary with the activity or chronicity of the case. In the active beginnings of caseo-pneumonic disease it may be advisable



Fig. 32—Extensive caseo-pneumonic tuberculosis in right upper lobe which has more recently spread to right lower and left mid-lung fields. The cross-infection on left side lies at a common site for metastasis while uncommon for a primary reinfection. Note the clear left apex and base.

to make films as often as once a week for a while whereas in chronic ulcerative cases intervals of three to six months are quite sufficient unless there is a distinct indication from some clinical change.

By a comparison of films made from time to time one may get a much more valuable conception of the character of the disease in each particular case and will frequently find on a subsequent film something that will help to explain findings on a previous film which was then difficult or impossible.

Perhaps the outstanding reason for making repeated x-ray studies at intervals is to detect at the earliest possible stage the presence of cavity formation. When cavities can be recognized at an early stage the possibilities of so managing the case as to result in healing is very much greater than when the cavity has become large and fixed. A few experiences of cavity in which one sees them develop from the earliest stage to the large fixed form will be of great

aid in teaching one to observe them early. I believe that it is commonly admitted that any of the radical measures instituted for the collapse and healing of cavities have much more promise of success if they are applied to the newly formed cavities than the old. Since cavities result from the evacuation of caseated areas it becomes necessary to follow all caseations to their final stage, whether they

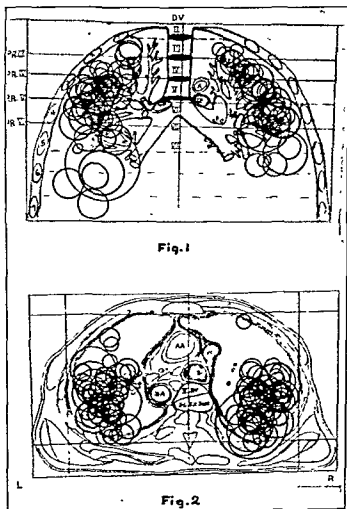


Fig. 33.—Reproduction from sketches by Sweany, Cook and Kegerris accompanying article on location of cavities in *American Review of Tuberculosis*, Vol. XXIV, page 574. Two hundred and sixty-eight cavities in two hundred and four patients were localized from stereoscopic films. The upper sketch shows graphically the predominant location in upper lobe peripheries. The lower sketch shows their almost uniform position near posterior chest wall.

become resting nodes, encapsulated fibrotic nodules, or centers of liquefaction and cavitation. Profuse expectoration at any time may be a hint which will lead to the demonstration of cavity.

Serial roentgen studies involve the making of numerous films. The economic factor entering into such studies will frequently create hardship on the patient

unless the roentgenologist is in position to coöperate in the follow-up work according to the patient's financial status. Frequently after a fluoroscopic glimpse one is justified in making a simple flat film from time to time. Attempts have been made to lower the film expense by substituting sensitive papers. These give fair results but are more difficult to handle in the dark room. Where the



Fig. 34.—Multi-form lesions occupy the entire upper right lobe. A nest of cavities in apex extend well below the clavicle. The larger patches of consolidation lower down undoubtedly contain caseated material but none shows dissolution toward cavity formation. The discrete character of the cavity walls speaks for a longer duration than the lower more active lesions.

lesions present maximum ranges of density no paper can be produced that will record them as well as the modern film. The situation demands a little more intelligent cooperation, economy and convenience.

(9) **Classification as to the Extent of Involvement.**—In a classification of this nature adopted by the Sanatorium Association in 1916 provision is made for utilizing the roentgen findings to some extent in separating the cases into

the three main divisions; "minimal," "moderately advanced" and "far advanced." For subsequent observations the rays are also utilized under certain stipulations in classifying cases as "arrested," "apparently arrested," "quiescent," "improved," and "unimproved." Without giving the entire text of the clinical data we will sift out all mention of roentgen findings and in some instances show



Fig. 35.—A round cavity with rigid wall lying in a right upper lobe extensively fibrotic. The lobe is retracted upward and the tracheal air column is displaced toward that side. During the length of time required for the formation of the dense fibrous material the cavity has failed to spill infective material to other lobes.

how they are used in conjunction with the clinical points. All x-ray findings are based on the study of stereoscopic films with or without fluoroscopic study.

*Minimal.*—A slight lesion limited to a small part of one or both lungs. No serious complications. The roentgen findings of a slight lesion are lessened transmission of x-rays in the form of poorly defined, light mottling or diffuse haziness interpreted as infiltration or conglomeration of tubercle, or more intense shadows of a well-defined, stellate, or fibrillar character interpreted as fibrosis, with or without opacities interpreted as calcification. The total volume of

involvement, regardless of distribution, shall not exceed the equivalent of the volume of lung tissue which lies above the second chondrosternal junction and the spine of the fourth or body of the fifth thoracic vertebra on one side.

It is emphasized that roentgen findings may be positive where physical signs are negative or doubtful, and that less frequently definite tuberculosis may exist without demonstrable roentgenographic change.



Fig. 36.—Right upper lobe cavitation with spontaneous pneumothorax limited in extent by adhesions at interlobar fissure. Every part of the lobe has collapsed more than the cavitated area although its walls are of only moderate thickness.

Where physical signs and roentgen findings are at variance a given lesion should be classified by the method revealing the greater extent or intensity. The letter R is used to specify roentgen classification and the letter P is used for the physical.

*Moderately Advanced.*—A lesion of one or both lungs, more widely distributed than under "Minimal," the extent of which may vary, according to the

severity of the disease, from the equivalent of one third of volume of one lung to the equivalent of the volume of an entire lung with little or no evidence of cavity formation. No serious tuberculous complications. Total diameter of cavities, if present, should not exceed 2 cm. The roentgen findings consist of shadows similar in character to those described under "Minimal," but more extensive or more intense, with or without areas of rarefaction interpreted as cavity formation. By cavity formation is meant single or multiple areas of rarefaction surrounded by dense borders.



Fig 37—An advanced case showing general type of reinfection from apices toward bases. Most of the caseated areas are small although the large upper right cavity (*A*) would indicate a previous large destructive process at one time. Pronounced proliferation has taken place in the upper thirds. Activity in mid lung lesions is evidenced by the "melted" appearance at margin of all lesions as from perifocal exudate. Fibrosis along mediastinal borders is pronounced.

*Far Advanced.*—A lesion more extensive than under "Moderately Advanced," or definite evidence of marked cavity formation, or serious tuberculous complications. In "Apparently Cured," "Arrested," and "Apparently Arrested" classifications the roentgen findings are to be compatible with the physical signs of a healed lesion.

In the "Quiescent" division the physical signs and roentgen findings are to be those of a stationary or retrogressive lesion and should remain so for two months. Under "Improved" it is stipulated that physical signs and roentgen findings are to be those of a stationary or retrogressive lesion. "Unimproved" cases will show physical signs and roentgen findings of an active or progressive lesion. Under the heading of a "Healed Lesion" it is required that roentgen

findings be compatible with physical signs of a healed lesion and must show clearing, fibrosis, calcification, or a stationary condition.

The foregoing resumé of roentgen definitions and requirements in classifying adult pulmonary tuberculosis are simply a small part of a general scheme of classification which, most properly, includes a predominance of clinical stipulations.

The x-ray enthusiast would say that the scheme has omitted considerable data which x-rays might easily supply and that the direct pathologic teachings of x-ray films could often be substituted, with benefit, for the clinical data in

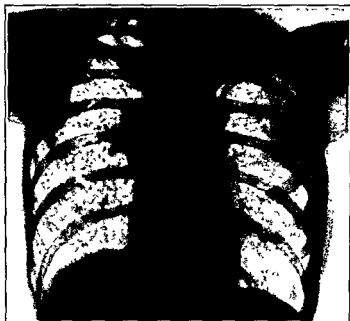


Fig. 38.—Widespread tuberculosis in which acino-nodose lesions predominate. One sees no healed areas and none which indicate massive caseation. Those at peripheries are diffusely exudative in type. No signs of cavitation. The nodular lesions are most numerous in the area around right hilum.

estimating the type and significance of involvement. He would support this, view by pointing out cases where serious caseous-pneumonic disease was attended by much less than the expected upset in health, cases where patient and doctor both were charmed with clinical improvement and let down on therapeutic measures. He would point out cases of very benign chronic proliferative disease which were kept on the most rigid régime for long periods mainly because of fear based upon the extent of involvement.

The facts are that in the practice of many individuals and institutions the x-ray is utilized as a guide in diagnosis, prognosis and treatment to a far greater extent than would be suspected by reading the classification or acknowledgments of any national associations. Such bodies are naturally conservative and naturally slow to modify the teachings of a life-time experience brought down to them from their fathers. It may be predicted that from time to time the national

organizations will choose to appropriate more of the roentgen evidence and incorporate it into their general scheme.

(10) **The Rôle of X-rays in Classification According to Predominant Type of Lesions Present.**—Depending on the number and virulence of the bacilli and upon the resistance of the patient the alterative, exudative and proliferative changes produced in the lungs are manifested by lesions of varying pathologic character in different individuals where the actual extent of involvement is quite similar. Large doses of bacilli gaining access to the lung of an individual of poor specific resistance produce a profound toxic destruction of tissue which



Fig. 39.—The many discrete nodular lesions grouped along the paravertebral border of both upper lung fields are mainly calcified and represent a favorable approach to complete healing in a rather severe involvement of paravertebral type. Fibrosis above left hilum may obscure outlines of enlarged glands.

may soon cause his death or may culminate in a localized area of tissue destruction to which he may ultimately succumb. On the other hand, small doses of bacilli well resisted tend to cause the minor infiltrative lesions which may run a smooth course to recovery. In these extreme types of involvement the lesions are physically and pathologically different and this difference often determines the prognosis and treatment. It so chances that by critical x-ray procedures one is usually justified in recognizing the various lesion types and by this method alone roughly classify them as belonging to one or another of the well known general pathologic divisions of tuberculosis.

Particularly in the last few years clinicians interested in pulmonary tuberculosis have employed the roentgen method to verify, amplify or correct their conception of the pathologic type of disease present as obtained by clinical exam-



ination and study. They have incorporated the x-ray findings into their records parallel with other data and have evolved a clinico-pathologic classification which is rather more definitive and significant than any clinical or pathologic classification when taken alone.

In 1931 Ornstein, Ulmar and Dittler presented a classification based on pathology from a clinical standpoint under the following four primary classes:

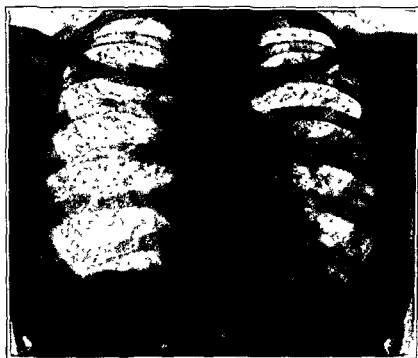


Fig. 40—Multi-form lesions of widespread distribution which vary as to age or degree of activity. Nearly all above the second rib show characters of complete healing. Many below this level show signs of activity. In left mid-lung area the activity is greatest as evidenced by the many lesions showing exudative characters. The largest area at hilum level must be watched for secondary signs of caseation. The right mid-lung area shows much resolution after a similar involvement.

1. Exudative Tuberculosis.
2. Exudative-Productive Tuberculosis.
3. Caseous-Pneumonic Tuberculosis.
4. Chronic Proliferative Tuberculosis.

1. In this classification the "exudative" type includes only those rare cases in which the x-ray findings are purely of an exudative character. The exudate is found to become resorbed in a few weeks, leaving almost no markings to indicate the central lesion. The patient is highly allergic and never very ill. Except for the clinical course and the occasional finding of bacilli the findings are compatible with a *nontuberculous pneumonic consolidation*.

2. In the "exudative-productive" type the first lesions are of an exudative character but the number and virulence of bacilli reacting on the individual of

adequate resistance fails to reach the climax of development known as caseation and in the succeeding stages shows a favorable resorption and fibrosis.

3. The "caseous-pneumonic" attack begins as an exudative affair but is much more severe so that the toxic action of the organisms is not halted at any stage before caseation. This caseation may be in foci no larger than the acinus



Fig. 41.—Definite enlargement in right peribronchial lymph glands with slight exaggeration of linear structures leading to base. The rounded, homogeneous appearance of the glands suggests active disease. In combination with clinical data it may be decided they are tuberculous but their x-ray appearance is uncharacteristic. A sufficient interference is definite gland enlargement.

or it may be of any larger size. Upon liquefaction and discharge a cavity is left which if small may heal or if large may persist and ulcerate. This caseous pneumonic group includes a large majority of chronic cases seen in the sanatorium or clinic and its manifestations are so variable that it deserves careful qualification and subdivision. The term merely calls up the picture of acute caseous pneumonia and the complications and sequelæ of caseation in later stages.

4. The "chronic proliferative" type is characterized by a predominance of linear and nodular fibrotic lesions with signs of activity strictly limited at any one time during a long progressive course. In this classification lies the acino-nodose type in which are seen the many nodular lesions of acinous size tending to fibrose, and the more common chronic proliferative type where small lesions



Fig 42—Enlarged right peribronchial lymph glands with nearhealed interlobar pleuritis. The glandular outlines are not discrete but matted in appearance. Pleural thickening rather than free fluid accounts for the interlobar density. The condition was thought to be tuberculous in nature. There was no x-ray sign of tuberculous involvement in the lung itself.

heal slowly with much scar formation in a succession of reinfections which traverse the lungs from apex to base.

Much can be said in favor of this classification. It has the logical basis of beginning with a type where simple exudative lesions predominate and ending with a type where the predominant change is fibrotic. In criticism one might point out that the purely exudative type is a rarity and fails to deserve classification parallel with the caseous-pneumonic types except in theory. Actually, the caseous-pneumonic division includes such a majority of the chronically sick

cases and manifests itself in such variety of forms that it merits an extensive subclassification and qualifying comment.

From a practical pathologic and clinical standpoint I believe that a classification based upon the presence or absence of caseation would be most helpful. Caseation is the one lesion which represents the climax of the severe infective



Fig. 43—A most uncommon case of basal tuberculosis in a young woman of twenty-seven years. A number of soft islands of consolidation are seen which have more or less rounded borders. The x-ray appearance is to be expected in metastatic tumor rather than in tuberculosis. Less pronounced changes were visible in left base. See Fig. 44.

onslaught and at the same time stands as the preliminary stage in that chain of events which includes cavity formation, ulceration and potential reinfection. The presence or absence of large caseations usually determines whether a case is relatively benign or malignant in character. It is impossible to review x-ray films without keeping foremost in one's mind the question of caseation as influencing the prognosis and treatment.

The "exudative," the "exudative-productive," and the "chronic proliferative" are relatively benign forms in which caseation is absent or very minor in extent.

Somewhere between the variables of "number and virulence of the bacilli" and "resistance of the patient" a resultant is reached in these types which lies short of the caseation climax. The term "exudative" suggests moisture and "proliferative or productive" suggests dryness or healing.

Caseation is a prominent feature in certain stages of those more serious forms of tuberculosis grouped under the general heading of "caseous-pneumonic." Pathologists subdivide it as follows:

Acute broncho-pneumonic  
Acute pneumonic phthisis  
Chronic ulcerative  
Chronic fibro-ulcerative



Fig 44.—The same case forty-four days later. Tubercle bacilli were now numerous in sputum. One may now see small patchy consolidations in left mid lung area which indicate numerous small foci of reinfection. Also some of the right basal islands appear fragmented. From a series of films in this case one can only infer a primary reinfection in the base with dissemination upward.

Because lung tuberculosis so often develops in impure or mixed types a critical pathologic classification is impractical and a rough approximation is used, based on the predominance of one or another type of lesions. When the disease is of pure type the clinical status of the patient will closely correspond to the usual clinical features attending the type. When lesions are of the mixed type the approximate pathologic classification made from the roentgen studies must be coordinated with the clinical study to correctly evaluate the patient's status.

I would not be able to suggest an A, B, C classification that would adequately express the roentgen findings in routine cases of pulmonary tuberculosis without adding to it an array of qualifications, exceptions and descriptive para-

graphs of essential value. Some suggestions as to features which should properly be covered in roentgen reports are outlined below:

- |                                      |   |
|--------------------------------------|---|
| Exudative                            | <ol style="list-style-type: none"> <li>1. Location and extent of simple exudate?</li> <li>2. Degree of clearing?</li> <li>3. Amount of final fibrosis?</li> </ol>   |
| Exudative                            | <ol style="list-style-type: none"> <li>1. Location and extent of small nodular involvement?</li> </ol>  |
| Productive                           | <ol style="list-style-type: none"> <li>2. Persistence of nodules at clearing; minor caseation?</li> <li>3. Degree of linear or nodular fibrosis?</li> <li>4. Signs of spread?</li> </ol>  |
| Chronic                              | <ol style="list-style-type: none"> <li>1. Location and extent of involvement?</li> </ol>  |
| Proliferative                        | <ol style="list-style-type: none"> <li>2. Tendency to result in linear or nodular fibrosis?</li> <li>3. Relative amount of fibrosis and newer type lesions?</li> <li>4. Exudative or caseative character of newer lesions?</li> </ol>   |
| Caseous-Pneumonic                    |   |
| (A) Acute                            | <ol style="list-style-type: none"> <li>1. Location and extent of exudative type consolidation?</li> <li>2. Evidence of large type caseated areas on clearing?</li> </ol>  |
| Bronchopneumonic                     | <ol style="list-style-type: none"> <li>3. Earliest type cavity formation?</li> <li>4. Large fixed cavity?</li> <li>5. Evidences of fibrosis?</li> <li>6. Evidence of atelectasis?</li> <li>7. Evidence of spreading infection?</li> </ol>   |
| (B) Acute                            | <ol style="list-style-type: none"> <li>1. X-ray findings of pneumonia involving one or more lobes?</li> </ol>   |
| pneumonic                            | <ol style="list-style-type: none"> <li>2. Spread before death to other lobes?</li> </ol>  |
| phthisis                             |   |
| (C) Chronic ulcerative               | <ol style="list-style-type: none"> <li>1. General extent of involvement?</li> <li>2. Number and location of fixed cavities?</li> <li>3. Caseation not the seat of demonstrable cavity?</li> <li>4. Evidences of fibrosis?</li> <li>5. Evidences of atelectasis?</li> <li>6. Evidences of recent spread of disease?</li> </ol> |
| (D) Fibro-ulcerative                 | <ol style="list-style-type: none"> <li>1. General extent of involvement?</li> <li>2. Number and location of fixed cavities?</li> <li>3. Extent of massive fibrosis or atelectasis?</li> <li>4. Visible caseated areas not evacuated?</li> <li>5. Evidences of recent spread?</li> </ol>                                       |
| Miliary Dissemination                | <ol style="list-style-type: none"> <li>1. Character of predominant miliary lesion?</li> <li>2. Presence or absence of older type lesions at some point in the lungs?</li> </ol>   |
| Collateral Changes and Complications | <ol style="list-style-type: none"> <li>1. Pleural effusion?</li> <li>2. Pleural adhesions?</li> <li>3. Pleural thickening?</li> <li>4. Pneumothorax?</li> <li>5. Pyo-pneumothorax?</li> <li>6. Massive atelectasis?</li> <li>7. Enlargement of peritracheal or peribronchial lymph glands.</li> </ol>                         |

#### (11). Parallelism Between Clinical, X-ray and Pathologic Findings.—

There are quite enough cases of insidious tuberculosis in which the disturbance to the patient is so slight that upon first examination or first discovery the disease has become well established and far beyond the minimal stage. And there are quite enough cases where vague symptoms bring patient to doctor and the doctor's careful examination fails to elicit sufficient signs of the tuberculosis which is present. This is due to no fault in our medical teaching and reflects no negligence on the part of patient or lack of skill on the part of examiner. It is an unfortunate lack of parallelism which exists in a minor number of cases between the symptoms, the clinical signs and the pathologic condition present.

Give credit to the careful clinician for his ability to suspect and find tuberculosis in the majority of cases. Many times he can predict the x-ray or

the pathologic findings with accuracy. But what careful clinician today has escaped the sad experience of passing over some of these insidious cases where the history and physical signs were insufficient and indeterminate? It is truly unfortunate that clicks and rales are not constantly audible in early tuberculosis and that minor depth consolidations often give no percutory findings. Every



Fig. 45.—These scattered nodules of simple calcareous density not accompanied by lesions of lesser density were discovered in films made for injured ribs. Such findings are pointed out as sufficient x-ray evidences of complete healing after a widespread involvement in a primary tuberculous infection. In this case the lesions were larger and closer together in the upper lobes.

careful clinician knows that this is true and often reserves his opinion until after the second or third examination.

Contrariwise, the findings of diffuse or localized bronchitis in cases with questionable history may lead a clinician to brand a case as suspicious and institute a prolonged and rigid régime for tuberculosis when in fact there were no tuberculous lesions present. The bronchitis was on a simple basis.

It is largely because of this lack of parallelism between symptoms, clinical findings and pathology that the x-ray has forged ahead during the last two

decades to help bridge the gap in pulmonary diagnosis. The x-ray attack is aimed directly at the demonstration of pathologic lesions and its value in this respect is just beginning to be reported in convincing manner percentagewise.

Witness the following excerpt from a recent article by Sampson and Brown, which must be predicated by the explanation that they have made a most particular and careful analysis of the x-ray findings in all their cases and have developed an almost faultless technic. "The incidence of the five cardinal diagnostic signs in 1367 cases diagnosed pulmonary tuberculosis from 1478 consecutive cases in the Trudeau Sanitarium:

Tubercle bacilli . . . .	61.5%
Rales . . .	68.5%
Röntgen ray .	99. %
Hemoptysis .	33.5%
Pleurisy .	12.0% "

This means at least that at Trudeau Sanitarium the x-ray is rated very highly as a diagnostic agent.

Because of the insidious character of the onset in many cases of tuberculosis and the frequent absence of diagnostic clinical signs it is becoming the practice to subject a relatively large number of patients to x-ray chest study in which there is very little suspicion of disease. This is entirely justified by the circumstances. It may be going too far to systematically radiograph all school children or all workmen in certain industries but the percentage of quiet tuberculosis picked up by this method is a little surprising.

The x-ray findings will be found to run grossly parallel to the pathologic findings through a rather wide variation of lesions. The limitations of the method have already been pointed out. Significant consolidations of the nodular type may be overshadowed and obscured by overlying pulmonary exudates, pleural exudate and occasionally by pleural or pulmonary fibrosis and pulmonary atelectasis. In the smaller type lesions separated by normal lung tissue the x-ray report will faithfully parallel the autopsy record. Some reasonable allowances must be made for failures in differential diagnosis.

(12) **The Term "Peribronchial Tuberculosis."**—During years of development in the combined use of clinical and x-ray methods of diagnosis there has developed the term "peribronchial tuberculosis." This has been largely applied to changes not at the lung periphery and not at the hilum but at the structures between. It is pointed out on x-ray films that the trunk markings are increased in width and density. Perhaps more of the small branches have been brought into prominence. Perhaps the increase is rather generalized in the trunk markings leading to the lower lobes. Perhaps at certain points along the radiating lines a few nodules may be made out.

On the basis of these changes a diagnosis of tuberculosis of the "peribronchial" type has been made and patients have been subjected to the same régime that is instituted in frank tuberculous cases. I believe that considerable harm has been done by accepting such a classification and believe that the roentgenologist has been fully as much to blame as the clinician. The diagnosis has in many cases been made where in a suspect case some findings of bronchitis



have been obtained and the clinician quite anticipates that x-rays will reveal tuberculous changes. When the exaggerated trunk markings are found the roentgenologist perhaps has unwillingly concurred in the inference that tuberculosis has been demonstrated although there is no peripheral consolidation present at any point.



Fig. 46.—Rounded calcified nodes scattered throughout all lobes of both lungs discovered in films made for a heart lesion. Patient admits no period of disability since childhood. Such shot-like calcifications are generally admitted to be the healed result of a disseminated tuberculosis although probably a primary manifestation of the disease.

Clinicians and roentgenologists who have followed these cases have found that from an x-ray standpoint the markings changed neither for the better nor the worse during a term of years. They also find that any other respiratory tract irritant may produce such an increase in the trunk markings and that congestion from incompetent heart may cause a most confusing increase.

The classification has been largely discarded in the best practice and yet it is a common occurrence today to see patients who have been "convicted" of

active tuberculosis on x-ray evidence of this character and who are searching for advice on climate and cure. I believe that pathologists do not recognize this as a discrete form of tuberculosis but that they speak particularly of involvement in the parenchymal areas and again in the glands about the trachea and bifurcation. The term "peribronchial tuberculosis" should be condemned and discarded until such a time as pathologists are willing to recognize it as an entity.



Fig. 47—Miliary tuberculosis in child of eleven years. Temperature 103.6° F. All clinical signs of activity. Films show only moderate amount of exudate about miliary deposits. Some lobular emphysema. No massive consolidation.

Increased trunk markings at the apex at a cone of infraclavicular infiltration have already been mentioned. A microscopic study of the tissue in these exaggerated trunks commonly shows lymphangitic infiltration or fibrosis but no tubercles.

An exaggeration of the individual trunk markings which extend to the base only, is not infrequently seen in connection with a few discrete or calcified

nodules as the end-result of a childhood tuberculosis. In the absence of any exudative appearance this also must usually be discounted as not significant from the standpoint of clinically active disease.

(13) **Basal Infection in Adults.**—Very infrequently a case may be found where the upper lung fields are perfectly clear and only in the base are there



Fig. 48—Miliary tuberculosis in adult. Same general character of change except that there is less amount of exudate about the myriads of foci present. The films better than the print show a more discrete character of lesion than in previous case.

changes which turn out to be tuberculous and probably primary at this point. Such cases may present the x-ray appearance of hematogenous metastases from distant sarcoma in that a number of roundish or pear-shaped consolidations lie scattered in the base with intervening pulmonary tissue rather clear and no sign of pleural fluid. The experienced roentgenologist will perhaps admit the possibility of such appearance in tuberculosis but may continue to insist that it is an appearance which is much more common in metastatic malignancy.

As tuberculosis it considerably simulates the infantile type which is not uncommon in young children and discussed more at length in another chapter. It is most interesting on account of its rarity.

An adult reinfection in the base following an arrested basal infection in childhood may give a mixed picture. The first infection may cause dense or calcified nodules and some dense fibrous-looking trunk markings leading to the base. The reinfection may produce bronchopneumonic patches of various sizes with or without pleural effusion. Basal tuberculosis in infants is properly discussed elsewhere.

Writers differ somewhat in their conception as to the frequency of basal tuberculosis but the prevailing opinion is that it is very rare, so rare that but few mistakes would be made if one assumed its nonexistence. In a recent article, Paul Default reviews a number of writers on this point. His article contains many of the following excerpts:

"Norris and Landis are very dogmatic: 'As I have repeatedly emphasized, tuberculosis is never primarily a basal condition. The fact that the physical findings are entirely limited to the base of the lung therefore excludes tuberculosis at once'

Fishberg asserts emphatically: 'Basal lesions in tuberculous patients are extremely rare; when they do occur, they are terminal phenomena when the diagnosis is beyond doubt. A lesion at the base, while the apex is free, should be considered as nontuberculous unless the sputum is positive as regards tubercle bacilli.' Speaking about tuberculosis in children, he clearly states, 'Chronic tuberculosis of the lungs in children of school age, when it does occur, affects the upper lobe almost invariably, and lesions in the lower lobes should not be considered tuberculous unless there are symptoms of toxemia and positive sputum.'

Hamman and Wolman, after a study of lower-lobe lesions, conclude, among other things, that it is unusual to have a tuberculous pulmonary lesion situated in the lower lobe alone, although occasionally such localization does occur.'

Garvin, Lyall and Morita claim that 'rales of long standing below the middle of the chest in the absence of heart lesions are almost as diagnostic of a chronic nontuberculous lung infection as rales of long standing at the apices or upper half of the chest are suggestive of pulmonary tuberculosis.' These authors believe, however, that 10 per cent. of all tuberculous lesions are located in the lower lobes.

Riesman, after reporting seven cases of basal nontuberculous lesions, says, "I am quite sure that a diagnosis of tuberculosis is often made in these cases of chronic cough with low continued fever; but if the chest is carefully examined, back and front, above and below, the peculiar, almost specific character of the disease will be discovered, and then the thought of tuberculosis will be no longer entertained."

According to M. Jacob, "lower lobe pulmonary tuberculosis without apical involvement is a rare condition."

Pancoast, discussing a paper presented by Dunham and Norton on basal tuberculous lesions, disagrees with these authors: "Primary basal tuberculosis

is frequently diagnosed by the more or less inexperienced, but it is a rare manifestation of the disease. I have seen very few cases of the type mentioned in the paper." A few authors, however, have taken the opposite stand and claim that basal tuberculosis is not as uncommon as generally thought.

Middleton claims that "evident signs of pulmonary tuberculosis may be overwhelmingly or entirely in the base." He admits, however, that such occurrences are the exception rather than the rule.

As already mentioned, Garvin, Lyall and Morita believe that 10 per cent. of all tuberculous lesions are located in the lower lobe. Dunham and Norton claim that basal tuberculosis is quite common in the negro and not uncommon in the white. To prove this assertion, they report 26 cases (admitted in two years in a 250-bed hospital) with lesions confined exclusively to the lower lobe. All these patients, however, showed signs of tuberculosis in other parts of the body."

Sante in his recent book, "The Chest," says in regard to the location of tuberculosis: "Nothing in the roentgenogram is characteristic of tuberculosis, not even the tubercle. The shadows of tubercles are called infiltrations, but to indicate tuberculosis they must be present in the apices before a definite diagnosis is permissible."

And again, under adult tuberculosis: "In the adult, roentgenographic evidence of tuberculosis appears first as infiltrations in the apices, or infraclavicular regions, just beneath the surface of the pleura. Only rarely does the infantile type occur in the adult. So-called primary lower lobe infection with tuberculosis is often of this type."

He further states: "Infiltrative tuberculosis may be primary in the lower lobes, but this is of very rare occurrence. When it does occur at this site the diagnosis can not be made from the roentgenogram alone since it bears no distinguishing characteristics from bronchopneumonia or secondary malignancy. Primary lower lobe tuberculosis is so rare that the diagnosis is not justified from any method of examination unless tubercle bacilli are repeatedly found in the sputum."

Fig. 43 shows roentgenogram occurring in my own experience from a proven case of basal tuberculosis. It was wrongly interpreted as a metastatic malignancy until temperature and bacilli-laden sputum developed. Six weeks later the basal nodes had broken up and patchy areas of reinfection were visible in the mid-lung areas (Fig. 44).

**(14) The Paradox of Positive Sputum with Negative X-ray Findings.**  
—Once every year or so there has been observed in my experience a case in which a positive diagnosis of adult pulmonary tuberculosis has been made by demonstrating tubercle bacilli in the sputum and to my amazement a set of critical x-ray films failed to disclose any sign or suspicion of parenchymal consolidation. This situation is very distressing and quite out of line with the usual experience which teaches that minor parenchymal infiltrations are to be seen very early in x-ray films, usually before sputum is available for microscopic study. Let just one case arise in clean cut form where repeatedly bacilli are found and the most critical x-rays are negative and one must either modify his conception of x-ray value or furnish some explanation for failure in the particular case at hand.

The further history of these cases also calls for an explanation. In each case after a few days or weeks the x-ray findings were positive. Undoubted patches of infiltration were easily visible and constant on the films. The showing at this time was just that expected in the first place. What more plausible conclusion could one reach than that the disease was present in the lungs at a stage where it cast off bacilli into the sputum without the x-rays showing it?

Several authorities claim that occasionally a focus of pulmonary tuberculosis develops in an upper lung field by the mechanics of a tuberculous lymph gland ulcerating into a bronchus and cite autopsy reports to support their theory. I have come to believe this to be the explanation for negative x-ray findings when sputum is positive.

Our conception of the chain of circumstances in the pre-bacillary period of most pulmonary tuberculosis includes the development of a colony with its toxic peri-focal exudate, a central zone of caseation of any size, liquefaction, and then evacuation in the form of sputum. The preliminary stages in this process involve an appreciable peri-focal exudate which is of physical size and character to be recognized in x-ray films.

Now when bacilli are present in sputum and the parenchymal findings by x-rays develop later the rational explanation is that an undemonstrable focus of tuberculosis in a peribronchial lymph gland ulcerated into a bronchus and an interval elapsed before it gained foothold in the lung itself. For this reason one should never neglect to make x-ray studies of the chest from time to time. A parenchymal lesion can usually be forecast.

Fortunately this paradoxical situation arises in so much less than 1 per cent. of the cases that it does not seriously upset the percentage accuracy of the x-ray method as applied to consecutive cases. I have been privileged to follow three such cases through stages of reinfection and healing. The location and appearance of the later pulmonary changes were the same as when infected by the usual route and healed as favorably.

It is predicted that more autopsy data will be accumulated showing gland foci rupturing into bronchus and into adjacent lung areas. The cavity one occasionally sees adjacent to the hilum suggests this manner of formation. It is simply unfortunate that x-rays are of no real aid in showing caseated foci in glands, neither do they show points of ulceration.

What x-rays show in these cases is the metastatic infection, when and if it gains foothold in the pulmonary tissue. It would be easy to speculate that in some other cases where on first x-ray study of the chest we show typical tubercloid deposits in the lungs the parenchymal changes may have developed by this route.

(15) **Summary of X-ray Value in Adult Pulmonary Tuberculosis.**—1. No inconsiderable percentage of the value of x-rays in connection with pulmonary tuberculosis lies in the negative x-ray result. With present day technic combined with the better understanding and confidence in the method both clinician and roentgenologist are satisfied to believe that when proper x-ray films show only normal structures the absence of pulmonary tuberculosis has been determined with a fair degree of certainty.

2. On the contrary when x-ray results show lesions in the lungs which are more or less characteristic for the commoner types of tuberculosis, or at least compatible with some of the less common types, then a more important service has been rendered, whether or not the findings can at once be verified by our older methods of examination. Parenchymal lesions are visible at a very early stage. The more one sees of tuberculous chest films the better he understands the character of the tuberculous lesion as portrayed. Because of overlaps in characteristics with some other diseases one must never forget that the x-ray findings are not pathognomonic.

3. In the differentiation of tuberculosis from other pulmonary disease the x-ray often plays an important rôle. The differentiation must be based on one's knowledge of the physical characters of the pulmonary lesions in a variety of diseases as expressed in terms of size, form, density, distribution and internal structural pattern. Insofar as the various lesions of tuberculosis can be recognized as differing in these respects from the lesions of other disease, just so far is one justified in carrying his differential observations. Differential diagnosis is treated in another chapter.

4. Because x-rays are capable of showing many intimate characters of the lesions, the method furnishes the best basis for determining the extent of involvement and the pathologic types of lesions present. Upon the extent of injury and the kind of tuberculosis present depends greatly the prognosis and the treatment. For the sake of scientific records and for summaries of therapeutic records some kind of classification is necessary and x-rays surely furnish part of the evidence upon which such classification may be based.

5. Classification as to the predominant type of lesions present carries with it an implication of malignancy or benignancy. Any survey of x-ray films teaches more. Films made at the "discovery" period show something of the patient's resistance to such invasion and any signs of healing to date. Studies made at subsequent periods are often invaluable by disclosing the actual "tendency to heal" present in the individual case or by disclosing a spread of the disease that calls for modification of treatment.

(16) **Mistakes Most Often Made in X-ray Diagnosis.**—In x-ray study of the chest for tuberculosis it is to be regretted that mistakes are not infrequently made in actual practice. While not presuming to criticize it is probable that mistakes of commission are rather more common than mistakes of omission. A common mistake has been pointed out with reference to the diagnosis of "peribronchial tuberculosis." For some reason roentgenologists and clinicians alike have seized on the finding of increased trunk markings as an indication of tuberculosis in the absence of any deposit in the lung peripheries. This may have been excusable in the day when x-ray findings had not been carefully oriented with the pathology, but today it should be seriously criticized.

In cases with temperature, loss in weight, or other symptoms best explained by a positive finding in the chest and when in such a case the clinical examiner finds evidence of localized bronchitis one has to become rather hard nosed to discount some prominent trunk markings and report the chest as negative for

tuberculosis when no changes are visible in the peripheries. One must become thoroughly convinced of the value of the negative film to do this.

Both internist and roentgenologist must remember that glandular tuberculosis is rather common and that much tracheo-bronchial tuberculosis is not to be determined by x-rays. One who has worked considerably with x-rays can hardly be convinced that tubercle bacilli are likely to be cast off from a true pulmonary lesion which will not show on x-rays.

With a firm conviction as to the appearance of the normal chest one may still report the pulmonary areas as negative when tubercle bacilli are found in the sputum even though the trunk markings show a simple increase in prominence.

Another kind of diagnostic mistake is sometimes made in estimating the stage of activity or healing. Certain rather discrete nodules of tuberculosis may maintain their physical characters without change for a number of years after which some activating influence causes a breakdown and spreads into other areas of the lung. One should be extremely cautious about pronouncing the lesions of tuberculosis completely healed on this account. For a long time they may be "arrested" in activity and finally become reactivated.

Mistakes of omission are relatively uncommon since present day technic brings to the experienced eye the smallest of parenchymal lesions. Whereas formerly it was perhaps excusable to overlook the presence of minor infiltrations in the peripheries adjacent to the shoulder of an obese patient, the films of today are not unlikely to fail in recording them.

Mistakes in differential diagnosis are often excusable for in certain cases no differentiation can be made by x-rays. It is perfectly possible that miliary metastasis from distant tumors and miliary nodules from silicosis may too closely resemble the miliary foci of tuberculosis for their critical differentiation. Other organisms invading the lungs such as blastomycosis, actinomycosis, vegetable molds and so forth may resemble the small nodular or more conglomerate infiltrations of tuberculosis. In the combination of tuberculosis with late silicosis or bronchopneumonia the recognizable characters of the tuberculous involvement may be obscured or rendered atypical.

Mistakes in pulmonary diagnosis which depend upon avoidable artefacts whether physical or chemical, and all such mistakes which depend upon improper placement of the patient during exposure are rather beneath the dignity of this discussion.



## CHAPTER XI.

# DIFFERENTIAL DIAGNOSIS OF PULMONARY TUBERCULOSIS.

BENJAMIN GOLDBERG.

### GENERAL CONSIDERATIONS.

The appearance of good health in an individual does not preclude the possibility of the presence of tuberculous disease and conversely, emaciation with a febrile disturbance and respiratory symptoms, does not always mean tuberculosis. Many patients of a plethoric type, well nourished and with a ruddy complexion, have been found to have phthisis, and many individuals have been seen with nontuberculous infections, neoplasms or metabolic disorders in whom respiratory symptoms caused the diagnosis of tuberculosis to be made. Hundreds of articles have been contributed to the medical literature from tuberculosis sanatoria, the general hospitals and Army examining stations showing the high percentage of errors made in diagnosing tuberculosis. While this points to the important fact that the profession is "tuberculosis conscious," it also shows the need for impressing upon the practitioners the important diagnostic criteria which will enable them to make a correct diagnosis in those nontuberculous conditions which produce manifestations simulating pulmonary tuberculous disease and which create pitfalls. The recognition of pulmonary tuberculosis does not rest upon any one single factor. It should be the result of a carefully taken history, a detailed physical examination, properly taken and interpreted roentgen films, and sputum examinations for tubercle bacilli. Constitutional symptoms that cannot be attributed to any other definite disease may at times be due to tuberculosis and should be investigated as being of such origin. One should also remember that pulmonary tuberculosis may be and is frequently coexistent with other diseases. Where a nontuberculous condition involves the respiratory tract and sputum is produced, it should always be examined for tubercle bacilli to determine the presence of the associated tuberculosis, if for no other benefit than to protect other contact individuals from such infection. Evidence of pulmonary pathology, even though it be of tuberculous origin, does not always indicate disease activity. Healed processes may leave residual pathology to produce physical signs, but only symptoms indicate activity of disease. One should remember that tuberculosis is not always insidious in its onset. There are acute forms which terminate favorably which must be recognized early, not only to institute proper supervision of the individual patient, but to allow the physician to seek out the source of infection and prevent other dissemination and disease production.

### IMPORTANT CRITERIA IN A POSITIVE DIAGNOSIS OF PULMONARY TUBERCULOSIS.

The consideration of a positive diagnosis of pulmonary tuberculosis should be built up around those factors which stand out as most commonly associated with this disease. Brown and Heise<sup>1</sup> for a number of years have made careful surveys of the histories of patients at the Trudeau Sanatorium and the compilations that have resulted have focused attention on the important diagnostic points to be sought.

A history of contact—intimate contact to an open case of tuberculosis—particularly of the caseous pneumonic group, where large numbers of tubercle bacilli are extruded with the sputum, is most important. One should not overlook the coughing relative with a supposed bronchitis or bronchial asthma when seeking a history of contact infection. Intimate friendship or relationship should not blind one to the possibility of the existence of tuberculosis in such friend or relative and should not prevent the suspicion of the presence of the disease and its diagnosis.

Pleurisy, occurring in the absence of an acute respiratory infection, particularly that pleurisy which is termed by many as idiopathic, may be the result of a sub-pleural tubercle and should always be suspected as being tuberculous in origin until disproved. Fistula in ano in a certain proportion of cases is tuberculous and whenever this condition is present a careful chest examination should be made.

Hemoptysis of one-half dram or more, coming from the lower respiratory tract, should be considered as due to tuberculosis until proved otherwise. While many other pathological entities may cause bleeding in the respiratory tract, tuberculosis is one which can be assisted toward a recovery and is also menacing to immediate contacts.

A consideration of the physical findings brings out the important fact that râles heard above the level of the third rib anteriorly or the fifth dorsal spine posteriorly, in the absence of acute respiratory disease, are usually due to tuberculosis. Ninety-five per cent. of lesions in this region, with persistent pathology, are tuberculous. One should, of course, utilize the various means of bringing out râles which may be "hidden." With the use of deep inspiration and cough, the persistence of such râles are important aids.

Roentgen films, indicating shadow densities, corroborating the localization of moisture found on auscultation in the parenchyma of the lung above the third rib, are most important. The roentgen film, properly taken, can delineate shadow densities indicative of disease, which previously were not demonstrated. This allows a more intensive study of the area involved. It is a sin of omission, even on the part of the most excellent diagnostician, not to utilize this important means of detecting pathology whenever its aid can be employed.

Tubercle bacilli in the sputum in greater numbers than one or two to the slide and in repeated specimens are important in determining the diagnosis. Some communities as yet receive a portion of their milk supply from herds of cows with tuberculous disease. The tuberculin reactors have not been excluded

and destroyed and, as a result, tubercle bacilli may be found in the milk, and, even though the bacilli are killed by pasteurization, they may still retain their staining qualities, become affixed to mucus in the oropharynx and be found in a sputum smear. We have also found tubercle bacilli in dental caries and in the exudate removed from tonsillar crypts in the absence of tuberculous disease of the respiratory tract. I repeat that the sputum from any respiratory disease should be examined if that disease persists. Some individuals with a positive sputum may only evidence bacilli in their sputum in the early morning and in a certain proportion of cases this early morning sputum is swallowed. Gastric lavage may yield the tubercle bacilli in specimens so removed later in the day. One should become conversant with the details essential in the proper examination of the sputum for tubercle bacilli and should also remember that degenerative types of tubercle bacilli, such as described by Much in his granular forms, may be present, even though the typical acid-fast types are absent.

The diseases which are important in the differential diagnosis of tuberculosis are listed below :

**Accessory Nasal Sinus Disease.**—This condition, which has become very prevalent, frequently causes a secondary hilar peribronchitis. Sometimes there are associated physical findings of a pneumonitis in the periphery of the upper lobe which may tend toward chronicity and with constitutional manifestations of toxemia resemble tuberculosis. The complaint of a head cold or nose and throat infection, the blowing of mucus from the nose or a post-nasal drip and tenderness on pressure over the frontal or maxillary sinuses is common. Roentgen films depicting sinus involvement and films of the chest which are negative for the typical shadow densities of tuberculosis are important. The sputum must always be examined for tubercle bacilli. Every year I see a number of patients with acute paranasal sinus disease and a concomitant pulmonary tuberculosis. Every patient with an acute or chronic upper respiratory infection and lower respiratory manifestations should have sputum examinations and a roentgen chest film made. Treatment and subsidence of the accessory nasal sinus disease is followed in a short time by clearance of the pulmonary manifestations, except in tuberculosis. Acute or chronic infections of the tonsils, adenoids, gums and teeth, with lower respiratory tract involvement, should also be managed diagnostically as are the sinus infections. A majority of the lesions resulting from the above mentioned infections, when they persist, tend to produce basal lung lesions and lesions limited to the hilar region. These should never be diagnosed tuberculous without a positive sputum. The incidence of tuberculosis in such cases is less than 5 per cent.

**Influenza and Allied Streptococcic Infections.**—This disease in its acute respiratory form may leave a variety of lower respiratory tract pathological manifestations, which may persist for some weeks and resemble tuberculosis. These are a hilar peribronchitis with a tracheobronchial or bronchopulmonary adenitis, occurring principally in the young; a peripheral pulmonary pneumonitis, single or multiple in small patches around the terminal bronchioles, or a pulmonary interstitial fibrosis.

Time is an important factor in the differentiation of these conditions. The *influenzal infections* tend to clear in the majority of instances within several weeks. The absence of tubercle bacilli in the sputum is important.

One should also remember that *fibroid or fibro-ulcerative tuberculosis* will at times have periods of activity, alternating with quiescence. During the periods



Fig. 1.—Basal bronchiectasis —saccular in the right, and fusiform in the left lung.  
(Courtesy Dr Willard Van Hazel )

of activity, toxin absorption may produce headache, backache, fever, weakness and cough. A diagnosis of influenza of a recurrent type is made and the attention of the physician in many instances may only be attracted to the tuberculous nature of the disease by the occurrence of a pulmonary hemorrhage. Roentgen films of the chest should be made of every patient with recurrent influenzal or other respiratory infections.

**Bronchiectasis.**—Bronchiectasis is usually secondary to acute or chronic respiratory tract infections, which allow a thinning of the bronchial wall. This,

after the strain of severe coughing, may produce a distention of the bronchus into fusiform, cylindrical or sacculated types. Occasionally traction from without is a factor in creating the dilatation. Only a few cases are congenital. The sputum is fetid or sweetish and is usually coughed up in large quantities, most frequently in the morning. It decreases in amount toward the afternoon and evening and again increases when the patient reclines or on retiring to sleep when postural change occurs. The sputum contains blood intermittently. When allowed to stand, it spreads in three layers—an upper, frothy, an intermediate, thin, turbid and usually greenish, muco-serous mixture, the bottom layer having a heavy sediment consisting of pus and other debris with Dittrich's plugs. The general nutrition of the patient is usually good, although a sallow and cyanotic color may appear. *Dyspnea on exertion develops. Club fingers and toes are common* very early in the disease. The physical findings are those of moisture in the area of involvement with signs of cavity formation occasionally. Roentgenography, after injection with an opaque substance—lipiodol—is most important in definitely delineating the location, extent and type of involvement. Dry bronchiectasis, with a dry, persistent cough, recurrent hemoptysis and evidence of fibrotic changes, is best diagnosed by pneumonography with lipiodol. Persistent, chronic bronchitis should be investigated for this type of bronchiectasis.

Chronic apical bronchiectasis is usually associated with pulmonary tuberculosis, but in the absence of tubercle bacilli on repeated examination, in the presence of a lesion resembling the chronic caseous pneumonic type, it should be suspected. Lipiodol injection through postural alteration will show the bronchial dilatation.

**Lung Abscess.**—Acute lung abscess usually occurs after an upper respiratory infection, pneumonia, surgical operations on the upper respiratory tract, the mouth, nose, tonsils, jaws, etc., and aspiration of foreign bodies. It may also result as an embolic manifestation from some focus of peripheral suppuration. *In the acute type the symptoms of cough, sputum and septic syndrome are usually followed by pain in the chest of a bursting type, with much pus—usually fetid and admixed with blood—coughed up.* The roentgen examination will show the abscess area. In the chronic non-tuberculous abscess, cough is more or less persistent; sometimes spasmodic. There is an abundance of sputum, which is frequently foul and admixed with blood from recurrent hemoptysis. A blockage of the bronchus draining the abscess aggravates symptoms. The sputum is negative for tubercle bacilli, but may contain the fuso-spirochetal or other organisms. Roentgen examination may disclose the abscess, which frequently has a fluid level. On several occasions I have seen chronic basal right lung involvement diagnosed as tuberculosis without a positive sputum having been obtained. The finding of bile in such sputum allowed the making of a diagnosis of an hepatic abscess, ruptured through the diaphragm into the lung, and draining through a bronchus.

**Chronic Bronchitis and Pulmonary Emphysema.**—This condition is due to bronchial irritants of various types, producing a chronic cough, cyanosis, with an expiratory dyspnea. The patient develops a barrel-shaped chest, having a hyperresonant percussion note throughout. On auscultation the expiratory

murmur is prolonged and medium or coarse moist or sibilant râles may be heard. Roentgen ray films show decreased shadow densities in the lung alveolar areas. This condition must be carefully differentiated from the chronic productive tuberculosis where a chronic bronchitis and compensatory emphysema exist.

**Pulmonary Syphilis.**—Syphilis of the lung in this country is considered a rare condition. Symmers, in 4880 autopsies, found 12 with pulmonary syphilis. Osler described 12 with pulmonary syphilis in 2800 autopsies. Lord found 1 case in 3000 autopsies. The French authors discuss syphilis as of more frequent occurrence, both clinically and postmortem. Pulmonary syphilis occurs in the secondary stage as bronchial mucus patches and as such was demonstrated by Ornstein and Myerson. Later gummata may occur and form cavities. Fibrosis, involving the bronchi, may produce bronchiectasis or the manifestations may be entirely interstitial. The value of the Wassermann test is questionable in determining this condition, inasmuch as 5 per cent. of the general population, including those individuals having tuberculosis, give a positive reaction. The absence of positive pulmonary tuberculosis criteria, especially a negative sputum, and the presence of a positive Wassermann test, should—when chronic lower respiratory tract disease is present—lead one to suspect pulmonary syphilis.

**Undulant Fever.**—Recently undulant fever occurring sporadically, with a chronic febrile course and leucopenia, has been diagnosed as pulmonary tuberculosis. The spleen in undulant fever is enlarged and the agglutination test of patients' serum with pure cultures of bacillus abortus in proper titre establishes the diagnosis.

**Pneumoconiosis or Dusty Lungs.**—There are four types of this condition which are given common recognition at this time—silicosis, which is due to silicon in sand, quartz, etc.; siderosis, due to iron oxide; anthracosis, associated with coal dust, or more frequently sand or rock dust adjacent to the coal vein (silicosis); asbestoidosis, caused by asbestos dust.

The history and duration of employment in exposure to one of the forms of dust capable of producing pneumoconiosis is important. Usually an average of five to eight years is required, although I have seen acute cases develop after six months of such exposure. The dust must be very fine—less than 10 microns in diameter—and the intensity of exposure to such dust, without the protection of an efficient respirator or face mask, is also important. The symptoms are cough, which is dry in the early stage, and later productive of profuse amounts of sputum. Night sweats and weakness are common. Dyspnea is evident as the pathology develops and becomes marked on the slightest exertion—even when resting in the advanced stages. The basal metabolic rate is increased proportionately with the extension of fibrosis and is caused by the anoxemia which results from alveolar fibrosis, preventing gaseous interchange. In some cases I have found the rate to be as high as plus 50 per cent., without any clinical evidence of thyrotoxicosis.

The roentgen findings are important and have been divided into three stages by Pancoast and Pendergass.<sup>2</sup> In the first stage there are accentuated hilar and peribronchial shadows due to the dust cells clogging the lymph channels. The second stage is usually noted in the right hilum and spreads in a generalized way.

A mottling occurs, due to fibrotic changes in the lymphoid cell deposits and lymph glands and resembles somewhat the appearance of pulmonary miliary tuberculosis. The linear peribronchial markings disappear in this stage. The third stage shows fibrotic extension to the bronchioles and surrounding tissue and ultimately the alveolar structure is involved, producing increased shadow densities of the linear and arborcal branchings. In these cases physical findings with signs of moisture over the apices of the lungs suggests a complicating tuberculosis.

**Foreign Bodies.**—Foreign bodies in the respiratory tract should be grouped into two classes: Metallic objects, needles, pins, tacks, nails, pieces of jewelry; and organic substances, such as peanuts, seeds, pieces of bone, peas, beans, teeth, etc. The organic objects rarely have to be differentiated from tuberculosis because they usually create a severe reaction, purulent pneumonia, abscess, etc., which may be fatal in a few days unless the object is coughed up or removed. Metallic objects may cause no reaction for several weeks or longer, except cough, wheezing or bronchial spasm, intermittent hemorrhage, etc.

The important factors in differentiation are a history of aspiration of the foreign body, physical findings, usually basal in location, roentgen findings indicating the object or when partial obstruction of a bronchus is present (Manges sign<sup>23</sup>). This is a one way valve action exerted by the foreign body: During inspiratory bronchial relaxation air passes, but on expiration it cannot pass out, thereby creating a pulmonary emphysema in the lung beyond that point.

**Heart Disease.**—Chronic myocarditis with decompensation in old age may create a pulmonary passive congestion, which, because of debility and the recumbent resting position of the patient, produces moisture in the posterior upper lung field. This may mask an existent tuberculosis or may be considered tuberculous disease. A careful examination of the heart and circulatory system to determine the presence of a cardiac decompensation and digitalis therapy with a slight change in posture of the patient will suffice to clear the passive congestion in most instances.

Mitral stenosis of a high grade may cause a hemoptysis and have associated cough, dyspnea and a mild toxemia, the result of an associated tonsillar or rheumatic infection, and thus be considered and treated as pulmonary tuberculosis. A careful examination of the heart should reveal the cardiac lesion. The increased size of the heart in the transverse diameter in mitral stenosis in comparison with the normal heart size in tuberculosis, and the presystolic or systolic murmur in the mitral area can usually be easily determined. Where decompensation is present, evidenced by basal pulmonary congestion and a congestion of the liver, digitalis therapy may be of assistance in causing the disappearance of such congestion. While the diminished incidence of pulmonary tuberculosis in the presence of mitral stenosis has been quoted in almost every textbook, one should not forget that a co-existing tuberculosis may occur in the presence of this type of cardiac disease. Freilich, in 1919, collected over forty cases at one time, under supervision in our dispensaries, of concomitant mitral stenosis and pulmonary tuberculosis with tubercle bacilli in the sputum.

**Bronchogenic Carcinoma.**—This condition occurs most frequently in males, approximately five to one, usually after forty years. The predisposing factors are exposure to coal-tar fumes, cobalt mining, dusty trades or association with recurrent bronchial infections and inflammations, such as influenza. Either lung is involved with equal frequency. The early recognition of this condition should be based on a persistent, irritative cough which does not respond to sedatives, with intermittent hemoptysis, sputum which may contain cancer cells, and negative x-ray findings. In an individual past forty this should



Fig 2—Generalized carcinomatosis of the lungs.

call for a bronchoscopic examination and biopsy. If the nodule grows and it remains localized so that it almost completely occupies the lumen of the bronchus, it may create the one-way valve action occasionally seen where foreign bodies have been aspirated, and then a pulmonary emphysema may occur in the alveoli beyond the malignant nodule. This produces an area of tympanitic resonance with a diminution of breath sounds; with complete occlusion of the bronchial passage, a localized atelectasis occurs, and the physical signs become more permanent. Pain in the chest and dyspnea are frequent. Dullness and flatness are found over the area of involvement with the extension of the tumor mass. Metastases to the lymph glands of the mediastinum and cervical region, axilla and brain are most common.



The roentgen findings, which very early are negative, later will show well demarcated nodular or diffuse tumor masses. These may be accentuated by diagnostic pneumothorax, or injection of the bronchus with an opaque fluid may show the bronchial obstruction. When extension to the pleura occurs, the lesser shadow densities may be obliterated by pleural thickening and fluid. Thoracocentesis will give a bloody fluid with cancer cells. With involvement of the parietal pleura, the intercostal lymph nodes may become enlarged and removed for biopsy.



Fig. 3.—Multiple sarcomatosis of the lungs.

**Primary Malignancy of the Lung.**—There is considerable debate as to whether carcinoma does develop primarily in the alveolar tissue or whether it occurs there as an extension of a bronchogenic cancer. While my clinical experience dictates the latter belief, I combine in this short paragraph a description of both carcinoma and sarcoma of the lung parenchyma. These cannot be readily distinguished by physical examination. Considering them separate entities, various writers state their incidence as only about 10 per cent. of the bronchogenic malignancies. They are frequently latent for some time and when they spread assume two types: A nodular multiple or single diffuse. Roentgenologically, the diffuse type starts as a small mass, spreading by the lymph channels and bronchi, invading and infiltrating a lobe or entire lung.

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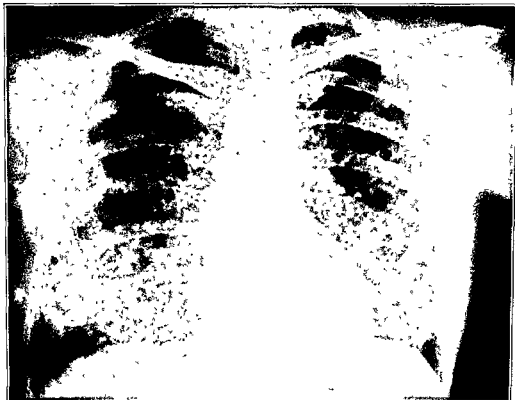


Fig 2—Generalized carcinomatosis of the lungs

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**Primary Malignancy of the Lung.**—There is considerable debate as to whether carcinoma does develop primarily in the alveolar tissue or whether it occurs there as an extension of a bronchogenic cancer. While my clinical experience dictates the latter belief, I combine in this short paragraph a description of both carcinoma and sarcoma of the lung parenchyma. These cannot be readily distinguished by physical examination. Considering them separate entities, various writers state their incidence as only about 10 per cent. of the bronchogenic malignancies. They are frequently latent for some time and when they spread assume two types: A nodular multiple or single diffuse. Roentgenologically, the diffuse type starts as a small mass, spreading by the lymph channels and bronchi, invading and infiltrating a lobe or entire lung.

The nodular type presents multiple nodules from the size of a pea to a walnut. They resemble metastatic involvement and metastasize very readily. Symptoms may be delayed for some time and the malignant mass discovered on routine examination. Loss of weight, weakness, dyspnea and ultimately, pain in the chest with cough and a blood-streaked sputum indicate respiratory involvement. The physical signs dependent upon bronchial blockage and atelectasis are compression and extension through the parenchyma and pleura. This produces pulmonary edema, congestion and bronchitis. Intra- and extra-thoracic metastases are common. Other primary neoplasms of the lung—chondroma, fibroma, osteoma and endothelioma are rare and only of pathological interest.

**Mediastinal Tumors.**—This group includes sarcomata, carcinomata, aneurisms of the aorta, persistent thymus, substernal thyroid gland, Hodgkin's disease and some of the more rare benign tumors, such as teratoma, dermoids and hydatid cysts. Not only is the differentiation of mediastinal tumors from tuberculosis important, but the differentiation of the different types of neoplasms is also important. Especially is this so as regards lymphomata of the sarcomatous or the Hodgkin's disease variety, which may, through radiology, be kept under control for many months or in some instances years. The roentgen ray examination offers the most important aid in the diagnosis of these conditions. The *anteroposterior and lateral view films should be augmented by fluoroscopic study* in these as well as in the oblique upright positions. In this way the competent roentgenologist can, in many instances, be of much assistance in locating the seat of the mass. The symptoms and signs caused by these tumors are largely the result of infection or compression of the structures contained within or adjacent to the mediastinum, trachea, esophagus, heart, aorta and its tributaries, bronchi, lungs, nerves, sternum and vertebral column. Metastatic lymph gland involvement in the axilla and cervical regions is common in the various malignant neoplasms and biopsy is the order when such involvement occurs. Routine hematologic examinations may be of assistance in diagnosing some types of tumors. Metabolic rate changes may be of assistance when this test is employed where associated manifestations of thyrotoxicosis are present and may allow of the diagnosis of a substernal thyroid. The *bruits over aortic aneurisms with tracheal tug and inequality of the radial pulse may be factors in diagnosing such aneurisms*. Mediastinal abscesses, secondary to retropharyngeal abscesses, or following infections resulting from the burrowing of malignant growths through the esophagus will give evidence of sepsis and will frequently rupture into the esophagus or trachea or will be found as a fluctuating tumor in the parasternal region or occasionally as high as the substernal notch, while abscesses developing from the vertebral column, most frequently cold abscesses, follow along the muscle sheaths and assume a fusiform shape.

**Actinomycosis** is caused by the ray fungus, which usually appears as yellowish granules found in the excretion from lesions caused by this organism. Pulmonary involvement occurred in approximately 10 per cent. of 680 cases collected by Sanford and Voelker.<sup>4</sup> A history of contact with cattle or the habit of chewing grain stalks or straw is important. The presence of a lumpy jaw and swelling about the neck or jaw is common. The pulmonary involvement

usually occurs in the lower lobes and may penetrate through the pleura, causing discharging sinuses through the chest wall. The ray fungus may be present in the sputum as yellowish granules or may be obtained through the excretion in sinuses through the chest wall or from the neck lesions.

**Blastomycosis** is produced by a budding yeast-like fungus. It is termed the "Chicago disease" because most cases have been reported from there. Clinical manifestations resemble tuberculosis, plus a pleurisy with effusion, and the findings in the lung are those of infiltration and consolidation. Skin lesions are very common. The last patient I saw had been under observation as a far-advanced pulmonary tuberculosis. Pus obtained from a skin lesion in this patient, examined with 10 per cent. sodium hydroxide—the usual routine—showed blastomyces. The budding fungus may also be found in the sputum.

**Sporotrichosis** is caused by a spore-bearing fungus, the most common in this country being *Sporotrichum schencki*, which has a wide distribution in nature in soil or vegetables, plants, flowers, fruits and grasses and on certain insects. Infection occurs through injury with contaminated thorn or splinter or contamination of an existent wound. Forbus<sup>5</sup> could only find ten cases of the pulmonary type in the literature. Complement fixation tests are positive and potassium iodide may be utilized as a specific therapeutically and therefore diagnostically.

**Streptothricosis.**—This is caused by a variety of fine, branching, spore-producing filaments, which can be differentiated through their biological and cultural characteristics. Pulmonary lesions, resembling tuberculosis, are present in a majority of patients. Differentiation may be made on the basis of metastatic involvement in other parts of the body and the finding of the fine, branching filaments, which are acid-fast, but may be discolored with alcohol after staining with fuchsin. Tubercle bacilli will not de-stain with alcohol. Certain fragmented forms which resemble tubercle bacilli must be carefully studied for differentiation.

**Coccidioidal Granuloma.**—This condition resembles blastomycosis, but proliferates by endogenous sporulation instead of budding. The organisms are spherical in shape, 15 to 40 microns in diameter, and have a double capsule. It is termed the "California disease," being most prevalent in that State. Males predominate, 94 per cent. being of that sex, as reported by Riesman and Ahlfeldt<sup>6</sup> in a review of 87 cases in the literature. The fungus in the sputum or discharge from glands may be grown on cultures in the presence of definite non-tuberculous disease.

**Aspergillosis.**—This fungus is usually a saprophyte, but may become a true parasite, according to Castellani,<sup>7</sup> and may thus cause a muco-purulent bronchitis with hemoptysis, closely resembling tuberculosis. The course is of long duration. The fungi, mycelial threads or the spores are found in the sputum. The infection is most frequently transferred from pigeons, by direct mouth to bill feeding. It is most common in France and Italy.

**Pulmonary Amebiasis.**—This is the result of a rupture of an amebic abscess of the liver through the diaphragm into the pleural cavity and then through the visceral pleura. There are large amounts of a typical, reddish-brown

sputum, which contains the *Endamaba histolytica*. The two patients I have seen were both previously diagnosed and treated as tuberculous.

**Hydatid Disease of the Lungs.**—Infection by the larvæ of the tænia echinococcus causes this condition. The larvæ are found most frequently in the dog and are rather rare in North America. Hooklets may be found in the fluid, which usually has a specific gravity of 1.009 to 1.015, is yellowish and non-albuminous. Symptoms are due to pressure of cysts, which may reach a size of four to five inches in diameter. A cyst may rupture into a bronchus and expel the contents—fluid, hooklets and daughter-cysts with severe bleeding and symptoms of asphyxiation. Rupture of the cyst into the pleural cavity, with signs of spontaneous pneumothorax, may also occur. Diagnosis may be assisted by obtaining the typical hydatid fremitus and is also aided by a precipitin test, utilizing the blood of the patient and hydatid fluid obtained from sheep. Complement fixation tests may be employed similarly or the hydatid fluid from sheep may be utilized by performing a Pirquet test through scarification of the skin.

**Trichiniasis** is due to infection with trichina spiralis, through the eating of insufficiently cooked or raw pork. Approximately 50 per cent. of the patients so infected show respiratory tract symptoms or signs. The outstanding manifestations are the onset with gastroenteritis, followed by myositis; a marked eosinophilia, and the presence of embryo of trichina in the blood or muscle tissue.

**Pulmonary Distomiasis.**—This is common in Asiatic countries, but only rarely is it found in the United States. The symptoms are cough, rusty, mucoid sputum, or bright red blood, pleurisy, bronchitis, parenchymal involvement, loss of weight, weakness, fever and physical findings of diffuse parenchymal involvement. The ova are 85 to 100 by 50 to 60 microns in size and are found in the sputum in large numbers. Rarely the worm 8 to 16 mms. long and 4 to 8 mms. broad and 2 to 5 mms. thick may be found coming from the respiratory tract.

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## SECTION C.

(Chapters XII to XVIII.)

### NON-SURGICAL TREATMENT.

Prognosis, Prophylaxis, Home Treatment,  
Rest, Exercise and Occupation, Diet (Plain  
and Salt-restricted), Medicinal, Symptomatic  
and Tuberculin Therapy.

## CHAPTER XII.

### PROGNOSIS IN PULMONARY TUBERCULOSIS.

BENJAMIN GOLDBERG, AND DONATO G. ALARCON.

*Prognosis* in pulmonary tuberculosis is dependent upon a complete knowledge, not only of the type and extent of pathology, but of many other factors that may influence the course of the disease. It has always been considered difficult to render a definite prognosis in this disease and this is more indefinite than the making of a diagnosis. The lack of proper consideration of the fundamental factors concerned in the immediate epidemiology of the disease, in addition to an intimate knowledge of different types of pathology, determined by re-activity of tissue and a failure on the part of many physicians to correlate physical evidence with roentgenologic findings, has prevented better knowledge as to the progress in any given type of pulmonary tuberculous disease. In the more serious studies of single or group cases of tuberculosis, it is not an uncommon practice to find various important considerations of the disease omitted when the question of prognosis is considered. Frequently there may be no thought given to certain individual factors affecting the patient. The peculiar diatheses, the social, the economic, the psychic reaction, as well as the intelligence quotient of the patient, are neglected when the treatment is being outlined to benefit him in his immediate environs. Prognosis has been considerably influenced in the past several years, by improvement in our mode of study as well as the better application of therapy, particularly surgical pulmonary collapse. The factors which are directly responsible for such improvement may be classified as:

1. The control of progress in tuberculous patients through serial roentgen examination.

2. The improvement in our knowledge of certain clinical types of pulmonary tuberculous disease, with particular reference as to the course and ultimate outcome in these various types.

3. The extension of knowledge of surgical collapse, not only to a larger number of physicians, but based on its application, to a larger group of patients.

Under surgical collapse we consider artificial pneumothorax, intrapleural pneumolysis, extra-pleural pneumolysis, apicolysis and extra-pleural thoracoplasty.

4. The increase in knowledge, which has been given to the general population, has been an important aid in the early recognition and treatment of tuberculous disease. This education has allowed better facilities to be established for the supervision of large numbers of tuberculous individuals, through dispensaries and the establishment of increased numbers of institutions for the hospitalization of such sick, thereby preventing further intimate contact, as well as giving the opportunity for intensive therapy.

Time and unexpected happenings, which latter we may term as "accidents," in the course of the disease, have to be considered as unavoidable stumbling blocks to accurate prognosis. The short term prognosis may be given with some certainty, but the prognosis in certain types of the disease over a period of years is yet an indefinite factor. The literature dealing with this phase of tuberculosis is rather meager and one-sided. Various authors attempt to utilize a single criterion or laboratory test as the basis for their prognostic declarations. This, we believe, is an error, and we again repeat that the clinician must endeavor to establish a personal equation in every case, which should be determined by all of the epidemiologic personal factors, a detailed study of the patient's diathesis, the clinical findings, the pathological type of disease, and serial roentgen examination to establish the trend the pathology takes. Prognosis is, therefore, the result of a complex equation, in which the various component elements are essentially variable, but usually indispensable in the final answer.

(a) *Individual Factors.*—The soil upon which the growth of tuberculosis depends has been for many years and is yet discussed as an important factor in determining the type of disease and its progress.

The arthritic diathesis, described in Bouchard's school, was originally considered as incompatible with tuberculosis. Individuals belonging to this constitutional entity, while they may develop tuberculosis, have some apparent resistance to the disease even in the presence of tuberculous infection. Contrariwise, the lymphatic diathesis makes individuals in this latter group more susceptible to tuberculous disease in the presence of infection. The arthritic type—broad, stocky, heavy-set, with decreased metabolic processes, highly concentrated food intake and diminished output—show evidences of accumulation of such substances as cholesterol, phosphates, etc., and deposition within joints, in secretory or excretory ducts of salt substances, the result of such metabolic processes. This diathesis is considerably influenced by habit, particularly dietetic, and is, we consider, one of the important differences in racial susceptibility to tuberculosis. Examples of this are seen among the Jews and Italians, with their high protein, fat and vegetable diets.<sup>1</sup>

(b) *The Acid Base Equilibrium*—The acid base equilibrium, termed B A, is being given some consideration in tuberculosis prognosis. This is especially stressed in dietetic research, as evidenced in the Gerson diet, and its attempt to alter such body chemical reactions. We would feel with Cannavo and Indovina<sup>2</sup> that the B A in tuberculosis is a factor in pulmonary respiratory function through its influence in varying the  $\text{CO}_2$  content and the  $\text{pH}$ . The "degree of alteration" of the B A discloses the alteration in pulmonary ventilation. "In incipient cases this would approximate normal. In extensive lesions the alkali reserve tends to increase, even though the  $\text{pH}$  is normal, while in advanced cases the alkali reserve is variable, with an increase in the  $\text{pH}$ ." Antemortem patients should always manifest an alkalosis. The factors involved in these gaseous changes have not as yet given definite evidence of their value clinically and we hesitate at this time in suggesting their utilization.

(c) *Cholesterolemia.*—Gilbert, Herscher and a number of other individuals have suggested that an increase in a cholesterol content of the blood was an

The viewpoints concerning the mortality in children under three years of age from tuberculosis have been considerably altered in the past several years. It was a common statement in and about the year 1900 that tuberculous disease at this age period resulted in a 100 per cent. mortality. These statistics have been gradually altered until the figures of Asserson indicate a low level of 59 to 44 per cent. within the age interval mentioned. The work of Gasul, in following a series of patients in the clinic of Pirquet, was also important in furthering the idea that tuberculosis in infancy is not necessarily a fatal disease. We might rather say that the finding of tuberculosis in an infant at this time calls for discovery of the source of infection and the immediate removal of the sick infant from that source. If the disease itself does not extend beyond the primary complex, the prognosis should then be considered good, for in only relatively few cases, due to the rupture of a caseous gland and early generalization, do fatalities occur.

The effect age has on the frequency of tuberculous disease in men and women, as mentioned above, is largely dependent upon associated factors concerned not only with physical reactions in the body, but with the conditions of these age groups in society. The tendency in early and middle adult life for excesses at work and at play and the habits as to foods determine to a considerable extent the reactivity of the body to infection, and while the evolution of the disease in this group depends on the presence of a previous primary infection and contact to repeated exogenous re-infections, we again emphasize that the habits in these age groups are important developmental factors.

In elderly individuals past fifty numerous infections with tubercle bacilli have occurred and have been overcome by the protective mechanism of the body. Life at this age is commonly sedentary; food habits are generally better balanced than among the young; and the tendency to lesions of chronic tuberculous type in the old is present. Alterations in the mechanism of the various glands of internal secretion may also be factors in controlling disease development and improving what we term "resistance." *We might say that an old man is not resistant because he is old, but that he probably is old because he is resistant.*

The age of an individual cannot be a deciding factor in prognosis, but must be considered in correlation with other facts, before mentioned, and especially in the matter of exposure to massive dose exogenous re-infections.

(g) *The Sex.*—Over a period of many years, tuberculosis was found with greater frequency among men than women, the principal reasons for the variance in incidence being given as the greater possibility of exposure to infection through more widespread opportunities of contact, occupations in industries supplying inadequate sanitation and ventilation in housing, long hours of labor which caused intense fatigue, and intimate contact without adequate physical resistance.

The great frequency of alcoholism and other forms of habitual dissipation in men were also mentioned. More recently our statistical evidence points to an increased frequency of tuberculosis in women, particularly in the younger age

groups. This has been attributed to the industrialization of the female group and also to various fads in diet developed because of esthetic ideas. It seems that the removal of the young woman from the fireside in her home to the outside world, and developmental factors in later adolescence, as influenced by certain sex gland elements, have played a more important rôle in allowing disease prevalence.

We would not say that sex in itself is an important factor in the prognosis of tuberculosis, excepting that the tendency is for women to seek diagnostic aid and treatment at an earlier period in the course of disease than do the men, and that persistence in therapy is found in the female group, who not being endowed with the responsibility of the male as to familial support, lend themselves to treatment more readily and over a longer period of time.

(h) *Education*.—Education is an important consideration, not only in the ability of the individual to recognize the fact that certain symptomatic manifestations call for an examination which may result in the recognition of the disease at an earlier time, but that the intelligence resulting from sufficient education may make the individual more amenable to the discipline so essential in the medical control of the patient. The more illiterate the patient, the more difficult it becomes to obtain a thorough understanding of the necessities of treatment outlined by the physician, including the hygienic arrangements in the home, the dietetic needs and the general training of individuals, which are the requisites for a favorable outcome. This is especially true for that large group whose treatment must be supervised in their own homes outside the sanatoria.

(i) *Racial*.—Repeated studies that have been made concerning tuberculosis as it affects the various races show that certain races, such as the Indian and Negro, have tendencies to develop the acute, grave types of tuberculosis. Other races, such as the Semites, to the contrary, seem particularly resistant and develop types of tuberculous disease which tend toward healing.

It is our feeling that the differences which occur in the reactivity of individuals in the different races to tuberculosis are dependent upon certain basic conditions which have to do largely with the following factors:

1. The delay or frequent lack of primary tuberculous infection.
2. Deficiencies or imbalances of diet which affect the bio-chemistry and create changes in the permeability which permit greater or lesser amounts of exudate to be thrown out about the infecting organisms.
3. Lack of sufficient education in sanitation and hygiene, resulting in poor and overcrowded housing, allowing of more easy and constant infection. Here, also, one should include the lack of common knowledge ordinarily held by the laity concerning medical conditions and an appreciation of coöperation with the medical profession.
4. The collective psychology of some of the races has been a most unfavorable criterion in the incidence of their tuberculous disease.

From a diagnostic standpoint it is most important to consider the race of the individual involved, but from a prognostic standpoint the factors enumerated above should be determining criteria as to the outcome.<sup>7</sup>

## CLINICAL TYPES.

The organization, from a pathological and clinical basis, of various definite facts in the reaction of the human host to tuberculous infection, has allowed the grouping of certain types into a classification which is of definite value in treatment, and therefore, prognosis.

Ornstein and Ulmar elucidate on this classification in chapter IX with great detail. Utilizing this classification, one should realize that, although tuberculous disease evidences different types of pathology in the same individual, a preponderance of one pathologic type may be present.

The acute benign tuberculosis that we are beginning to see more of is largely due to a lessened distribution of tuberculous infection early in life and a primary infection delayed so that it occurs in many instances during late adolescence or adult life. It may also be an epituberculous manifestation. This type of disease heals spontaneously in practically every case and its recognition, after a brief period of observation, should allow the making of a good prognosis.

The exudative productive tuberculosis also offers a good prognosis, but its differentiation from some forms of the caseous pneumonic disease is difficult in instances, except after a more prolonged period of observation.

The caseous pneumonic tuberculosis is the malignant form of the disease—the caseous material containing tubercle bacilli usually in large numbers so that extension of the process by continuity or by endogenous reinfection may take place. In this group we find the various types of disease, from the acute to the chronic, including acute pneumonic phthisis, acute bronchopneumonic tuberculosis, fibro-ulcerative tuberculosis and chronic fibroid tuberculosis. Healing in this group depends upon the control of the disease process by marked scar tissue formation. The prognosis in this group is usually serious and the patient should be given the benefit of any one of the various forms of collapse therapy indicated wherever such therapy can be applied. The control of the disease process in this way improves the prognosis.

The chronic proliferative type of tuberculosis produces a scirrhus disease which progresses despite therapeutic endeavors, the patient living for many years and ultimately dying of some intercurrent infection or concurrent disease.

**The Relative Value of Physical Signs and Symptoms.**—(a) *Fever.*—The temperature, carefully and accurately studied, is a matter of first importance in the prognosis. A febrile reaction which persists, despite continued general rest, good diet and satisfactory surroundings, in association with the other forces in our therapeutic armamentarium, usually signifies an increase in disease evolution, and is a most important symptom of disease activity.

An afebrile course should, on the contrary, not be considered as definite proof of inactivity of the disease. Physical exertion or exercise will usually, in the presence of active disease, create thermal reactions within the body. One should most carefully study temperature changes affected by exercise and attempt to correlate such changes with physical findings.

(b) *Cough.*—Cough is not of a definite or constant value in determining the presence of active disease. Residual pathological processes, bronchiectasis,

adhesions, etc., may be factors in the production of this symptom without any serious disease concomitants. The presence of a severe cough may be a factor in disseminating endogenous infection or in causing a break in a fibrous wall and thus allowing disease extension.

(c) *Dyspnea*.—The patient with an extensive bilateral disease, where a considerable amount of alveolar structure has been replaced, may suffer dyspnea because of a diminution of pulmonary function in gaseous interchange. Dyspnea may also be found as the result of severe toxemia in acute exudative lesions of the caseous pneumonic type or in temporary bronchial obstruction where it may be caused by a massive atelectasis, in spontaneous pneumothorax, or in massive pleural effusions. Miliary tuberculosis, as it develops, produces this symptom as one of its important manifestations. Dyspnea may rarely be a temporary psychic disturbance. The correct interpretation of the underlying factor in its production determines the seriousness of the condition, which may be a prognostic omen

Such conditions as spontaneous pneumothorax and miliary tuberculosis are known to have almost invariably a fatal termination.

(d) *Sputum*.—It has been the experience of those who have observed large numbers of patients with tuberculosis that the amount of sputum and its tubercle bacillus content are most important indices in estimating a prognosis. The amount of sputum in relation to other symptoms and physical signs, as Leuret and Lamothe<sup>8</sup> have pointed out, may allow one to determine the course of the disease. A decrease in the amount of sputum, with a decrease in its tubercle bacillus content, shows a tendency to healing. Fluctuations in temperature, associated with fluctuations in the amount of sputum, indicate insufficient drainage or opening of new disease foci. A constant decrease and stabilization of sputum may be taken as a stabilization of the disease. The continued absence of tubercle bacilli in the sputum in the course of healing is a most favorable sign.

(e) *The Pulse*.—A pulse rate over ninety, not associated with other cardiovascular or metabolic diseases, should be interpreted as the result of activity of the lesion. Patients in whom such a tachycardia disappears on bed rest usually have a regression of their pulmonary lesion. Even though the febrile reaction abates and apparent favorable progress toward recovery in the pulmonary lesion is manifesting itself, a persistent tachycardia, in the absence of other disease concomitants, should always cause one to hesitate in giving a favorable prognosis.

(f) *Blood-pressure*.—Variations in the blood-pressure can be considered the result of toxic phenomena, associated with the disease or general body activity or psychic reactions. Individuals belonging to the neuro-vegetative type have instabilities, principally of the hypotension variety. Those belonging to the arthritic diatheses usually have a hypertension and, as mentioned above, offer a better prognosis than those with a low tension, the result of damage to the cardiac muscle from prolonged toxemia. With a tendency to an improvement in the condition of the patient, one usually finds a corresponding improvement in the vascular tension.

(g) *Anorexia, Loss of Weight and Asthenia.*—These are symptoms of rather elementary significance which, if they persistently continue, point to a gradual loss in the ability of the individual to combat his disease successfully.

Anemia may be associated as a factor of asthenia or follow recurrent or severe hemoptysis. In some instances a pseudo pallor, which is not a real anemia, may cause concern. Hematologic studies should be made to determine the real presence of this condition.

(h) *Râles.*—Among the physical signs the increase in the number and findings of the moist râles is important. Such findings, in association with other manifestations of disease activity, are an aid in showing disease progression.

(i) *Pulmonary Cavities.*—The presence of true pulmonary cavities, not to be confused with annular shadows produced by emphysematous blebs or cellular zones of infiltration, is an important consideration in the prognosis. True cavities represent the results of caseation and the extrusion of the caseous material through a draining bronchus. Classified pathologically into the smooth wall and shaggy wall types, small and large, their presence and type should be determined and carefully studied by serial roentgen films and examinations to determine the number of tubercle bacilli contained in the sputum. In the shaggy wall types, found in the serious caseous pneumonic disease, with myriad numbers of tubercle bacilli thrown off, cavities are dangerous in producing extension of the disease, through endogenous reinfection, and metastatically to other organs. These latter cavities should be considered most seriously in offering a prognosis and, as suggested by Jacquerod and Pinner, they determine the immediate need for active collapse treatment. The location of cavities is important. Those located posteriorly are more difficult to treat, as are those which have thick walls and are located occupying extensive areas at the apex or base of the lung.<sup>9</sup>

(j) *The use of roentgen films* in making serial studies of patients with tuberculous disease has given considerable information. The roentgen film, properly taken and interpreted, yields information as to the extent and type of pathology which the physical examination very frequently cannot give. One must learn to differentiate between extensive shadow densities, caused by benign types of pulmonary tuberculosis, and caseous pneumonic or malignant types, which may be more limited in their area and yet which latter offer a more serious prognosis. The serial roentgen study over months, which indicates an extension of the lesion originally visualized, is, of course, an important factor and may cause the giving of an unfavorable prognosis. Conversely, resorption of exudates originally seen, with restoration of the normal lung parenchyma, interstitial changes evidencing a walling off of a lesion, the disappearance of small annular shadows, which careful study has interpreted as cavities, should be considered as favorable indices.

(k) *The Number and Type of Tubercle Bacilli as they affect Prognosis.*—Tubercle bacilli are not constantly present in the acute benign types of pulmonary tuberculosis nor in the chronic proliferative types. While the benign types usually go on, as above stated, to a favorable termination, the chronic proliferative type may persist in its invasion of pulmonary tissue over a period of many years to a fatal termination. This contrast brings out the fact that the number of



bacilli in the given case may not determine the prognosis. However, in the caseous pneumonic types of tuberculosis, large numbers of tubercle bacilli are usually found, but with a gradual improvement of the patient, determined by symptomatic, physical and roentgen film evidence and a gradually decreasing number of tubercle bacilli in the sputum over a constant period of time, such a decrease may indicate the healing of the tuberculous process. The long and granular forms of tubercle bacilli may evidence lytic processes—the result of destruction by certain body enzymes—or a lessened virulence of the organism.<sup>10</sup>

(i) *Special Blood Reactions.*—At this time there are three tests which seem of interest because they have received confirmatory conclusions from a number of authors. These are the sedimentation rate, the leukocytic index and the Verne's test. All three of these procedures rather parallel the information in their results. They yield information concerning the degree of activity of the tuberculous process quite accurately, but this information relates only to the time of the test and not to a period weeks or months hence. It is, therefore, important in utilizing these tests that they be repeated at frequent intervals to determine whether the curve plotted from their results continues favorable. The complement fixation and other serological tests, in our experience, have no definite value prognostically and we have had to disregard some of the isolated favorable claims for their use. The Loewenstein method of determining a tuberculo-bacillema is as yet in a period of preliminary study. Many conflicting reports are at this time in the literature concerning the findings. It does not appear to promise any aid prognostically.<sup>11</sup>

(ii) *The Tuberculin Reactions.*—Tuberculin has a definite value from a diagnostic standpoint in determining the presence of tuberculous infection, which infection has established a reactivity of tissue; as the result of such sensitization it may also in certain instances be of value prognostically. This value in prognosis is especially seen in the hyperallergic types of tuberculosis where extensive exudative processes are the rule. Such processes may be found under a variety of conditions. First, they may be seen as perifocal reactions with symptoms of only a most moderate degree and roentgen findings indicating extensive involvement. They may be found in the extensive exudative types of the acute benign tuberculosis, and also associated with exudative productive types, and in fewer instances, in the caseous pneumonic type of disease. In this latter type the presence of a severe local reaction, utilizing the Mantoux or the Pirquet tests, will usually indicate that a considerable amount of the shadow density, as seen on the roentgen film, is of a simple exudative type which, if given sufficient opportunity, will resorb, leaving only the destructive portion of the lesion as the residual process.

Prognostic utilization of tuberculin in this way is of accessory value in determining indications for therapy in the various types of tuberculous disease. Where the local reaction with tuberculin is very slight and limited in its extent, one cannot apply any special value to its importance from a prognostic standpoint. The negative tuberculin reaction in the presence of advanced tuberculosis, with moderate or extensive involvement and a severe toxemia, may indicate an anergy which is frequently a precursor to a fatal outcome.

The reactions of Widbolz, and the Diazo reaction of Ehrlich, as yet mentioned by a number of workers in this field, have no prognostic importance.

(n) *The Economic Status of the Patient.*—This is a most important consideration, inasmuch as it involves all of those essential factors in treatment which must be provided to give the patient adequate care. Fortunately, as we have stated in our chapter on the home treatment, governmental agencies in most civilized countries have made provision, which is fairly adequate, to surround tuberculous individuals with the requisites for proper treatment. In instances where the patient remains in his home, refuses to ask for assistance, and does not, under such circumstances, seek the aid of the public agency, the disease may become advanced to such a stage that the ultimate outcome can only be unfavorable.

**The Possibilities of Treatment from the Point of View of Anatomical and Clinical Development, as it Affects Prognosis.**—In giving consideration to the possibilities that exist under this heading one should include:

1. The evolution of the lesion and its approximate age, so as to determine whether sufficient progress towards resorption or organization and healing is taking place.

2. Unilateral or bilateral lesions; the extent and type of each, which determines the indications for various forms of therapy.

3. The tendency towards fibrous tissue formation, as evidenced in the physical and roentgen findings, signifying an attempt at localization of the lesion with a healing tendency.

4. The presence of adhesions, preventing collapse of cavities and making necessary the radical type of pulmonary collapse.

5. The presence of complications, both pulmonary and extrapulmonary, which may affect the ultimate outcome.

We would not enter into any more detailed discussion of these factors, inasmuch as that would involve a further exposé of therapy, which is adequately given in special chapters in this book.

**Complicating Disease Conditions as they Affect Prognosis.**—We should mention those complications which develop within the thoracic cavity, which are due to and associated with the pulmonary tuberculous disease. Those of serious nature are spontaneous pneumothorax, tuberculous empyema, and involvement of the soft tissues or the bony structures of the chest wall, which we sometimes see as an extension of an empyema.

(a) *Extrapulmonary Tuberculosis.*—In recent years the concept of the seriousness of extrapulmonary tuberculosis has been considerably modified. Tuberculous enterocolitis, the most frequent complication of pulmonary tuberculosis, which some years ago was considered a fatal complication, today, in a large proportion of cases, through proper treatment, may be healed.

(b) Tuberculous laryngitis, which was also given a 100 per cent. rating for mortality two decades ago, is now satisfactorily treated, especially in those instances where the pulmonary lesion is of the type that can be controlled by collapse therapy or heals because it is of a benign type.

The severe lesions of an ulcerative type, appearing in the oropharynx or larynx, in the latter stages of the disease, which evidence an inability of the tissue to fight infection and are seen as indications of the moribund character of the individual, portend a certain fatal outcome.

(c) Tuberculosis of the kidney and other organs in the urogenital tract influence the pulmonary lesion to a lesser degree than the other extrapulmonary forms and here, too, rationalization of therapy, through the use of ultraviolet light and certain dietetic restrictions, has been of special avail.

(d) Bone tuberculosis, skin tuberculosis and glandular tuberculosis are usually localized forms of the disease, associated with those types of pulmonary tuberculous disease which tend toward chronicity and therefore allow of the healing, not only of the primary pulmonary lesion, but of the extrapulmonary process.

(e) Miliary tuberculosis, either pulmonary or general, always has a grave prognosis.

(f) Tuberculous meningitis is fatal in practically every instance. We have seen several cases recover and there are some reports in the literature, but these are exceedingly rare exceptions.

**The Pulmonary Complications of a Nontuberculous Nature.**—The acute respiratory infections, such as influenza, acute bronchitis, bronchial and lobar pneumonia, may tend to aggravate the tuberculous lesion when the pneumonic involvement of the acute infection invades the zone of tuberculous involvement and, by creating new exudates, allows an extension of the tuberculous process, forming, in many instances, the condition termed "unresolved pneumonia."

The other factor involved in such infections is largely a mechanical one, which has to do with the stress and strain of coughing, allowing a dissemination of tuberculous infection into adjacent pulmonary tissue, or creating breaks in thin fibrotic walls so that tuberculous caseous material may extend into new tissue.

Bronchiectasis, lung abscess, pulmonary gangrene and other infections of a similar nature may also enter the above category. Pneumoconiosis of a silicotic type frequently has tuberculosis associated with it. Whether the tuberculous lesion preceded the development of the pneumoconiosis, or the tuberculosis developed subsequent to the pneumoconiosis cannot be determined in many cases. The tendency to an increase in the interstitial tissue and fibrosis in pneumoconiosis, especially in chalicosis, would seem to warrant a beneficial effect upon an existent tuberculous lesion.

Malignancy of the lung, principally in the form of bronchogenic carcinoma, rarely develops as a result of the destruction of the lining bronchial membrane from tuberculous disease, but may be an independent concomitant and may effect the tuberculous process by its destruction of the vitality of the patient during its growth into new tissue structures.

All other neoplastic growths have their own prognostic significance and they usually portend in themselves definite prognostic influences into which tuberculosis does not enter.

**Extrapulmonary Nontuberculous Involvements as they Affect the Prognosis in Pulmonary Tuberculosis.**—Diabetes is of special interest here. Since the advent of insulin, with adequate dietary supervision most of these patients can have their diabetes controlled, so that the prognosis is to be determined by the tuberculous pathology as ordinarily seen, without the diabetic complication. There are instances, however, in tuberculosis where insulin does not seem to control the diabetes adequately and increasing doses of insulin have to be utilized because of a decreasing carbohydrate tolerance. This is most evident in cases that are severely toxic and of a progressive caseous pneumonic type, frequently bilateral, so that collapse therapy cannot be done to control the tuberculous disease and its toxemia.<sup>12</sup>

**Tuberculosis in Pregnancy.**—The concept of this problem is also quite different at this time from that which existed only a few years ago. The gravity of a pregnancy complicating tuberculous disease has always created a pessimistic outlook and the suggestion, which we do not recommend, of an early interruption of conception. Studies which have been carefully and completely made in the past several years by Schulte, Rhonhof and Hansen,<sup>13</sup> and more recently by others in this country, indicate that the deciding factor in the outcome of these associated conditions is based on the type and extent of tuberculous pathology. Benign tuberculosis is not aggravated by pregnancy. The exudative productive types only rarely seem to show increases in the exudate and even then tend to resorption. The caseous pneumonic group have approximately the same mortality with pregnancy as without it, and again this mortality depends upon the ability of the phthisiotherapist to control the disease by the usual therapeutic régime associated frequently with collapse therapy.

**Tuberculosis and Marital Life as it Affects Prognosis.**—This deals principally with the economic responsibilities of the male, or the household duties of the female, which may, through psychic disturbance or physical fatigue, create barriers to the goal of healing. Marriage of the tuberculous should be avoided, not only because of these aforementioned facts, but because of the additional psychic disturbances and physical fatigue that come with sex life.

**Extra-individual Factors as they Affect the Prognosis.**—The tubercle bacillus: The three most common types of tubercle bacilli that live close to the human host are the human, the bovine and the avian. Infection of the human host with the latter is unusual and, while we mention it because of its common occurrence in certain foodstuffs, namely fowl, its incidence as a causative factor in human disease is rare. The bovine type of bacillus, which several decades ago, because of its wide distribution in common articles of food, milk and meat from cattle, was an important factor in the production of tuberculous disease in the human, is also becoming more rare in its incidence in the United States. Tuberculin testing of cows and the destruction of those found diseased, plus pasteurization of milk, has done much to eradicate this type of infection. It does, however, still occur in this country and in many other countries is found with a greater degree of frequency. For many years a controversial subject, we feel that some pulmonary tuberculosis and much of the extrapulmonary tuberculosis was the result of infection with this type of the bacillus. The milder forms of the disease

have been attributed to infection by the bovine organism, but transmutation through residence in the human host in many instances changes the morphological type so that it becomes difficult to differentiate, not only the organisms, but the disease reactions they produce.

The human type of bacillus is considered the most virulent of the group. The quantity of infecting organisms seems rather important. The virulence, while it may be controlled through attenuation, is a debatable factor, inasmuch as in individual cases the reactivity of the tissue, as influenced by the biochemistry of the human host, is a factor in the inflammatory change that may or may not follow inoculation.

### OTHER FACTORS.

(a) *Social Economic Conditions Affecting Prognosis.*—Major upheavals in the routine of society, such as war, may upset the entire life cycle of human beings in the countries involved. This, affecting the mental tranquillity of such individuals and limiting the dietetic needs—a condition which existed within the Central Powers of Europe during the World War—doubled, tripled and quadrupled the mortality rate in communities where previously tuberculosis had been considerably on the wane.

(b) *Nature of Work.*—The type of occupation to which the individual finds it necessary to return is often a deciding factor in his ability to maintain his health reserve. Hard shipping labor in the course of a healing process may be the exciting factor in provoking a reactivation of the disease. This should be most carefully guarded against.

(c) *Reinfection After Arrest of Disease.*—While danger lurks in endogenous reinfection in individuals who have active or latent tuberculous processes, the patient who has made satisfactory progress toward recovery must be protected against new exogenous reinfections. One must make certain that the patient is not returning to contact with an old fibro- or fibro-ulcerative tuberculous individual.

(d) *Disease Epidemics.*—Epidemics of diseases, particularly respiratory diseases, seem to be factors in increasing the extent of active tuberculous lesions already existent, or activating dormant lesions walled off or in the process of healing. Caution in the protection of the factors engendering good health, will also be valuable in preventing an increased incidence of reactivation in the tuberculous.

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## CHAPTER XIII.

### PROPHYLAXIS.

BENJAMIN GOLDBERG

#### INTRODUCTION.

The prevention of tuberculosis is as yet a complex problem, even though our increased knowledge concerning the control of the infecting organism and the soil upon which it is grown seemingly is clarifying the situation.

The belief for many years has been that a primary infection with, or primary disease caused by, tubercle bacilli produced a sensitization to further infection with that organism, and when such reinfection took place this sensitization operated as a protective mechanism to localize the disease and prevent extensive ravages in its host. This thought promulgated the idea that infection of human beings should therefore be allowed, to further the development of the protective mechanism. Associated with this, the idea was also expressed that the original focus of disease, developing from the primary infection, was the source of disease in later life when changes in the human body, incidental to alterations in body resistance, allowed the activation of such latent disease foci containing dormant bacilli.

Within the past several years our experience in observing large numbers of tuberculous individuals in urban communities, as well as the observation of competent pathologists at the postmortem table, evidences facts that vary from the above. We have learned that the original, or primary infection, producing the primary disease, results in a healed-out process in a majority of instances and only infrequently is the cause of an endogenous reinfection or an early generalization. These two latter conditions are almost mechanical in their occurrence, inasmuch as they most frequently result from the rupturing of a caseous gland in the course of the primary complex.

We have also learned that the sensitization which has resulted from this usual innocuous primary infection does not always function as a protective mechanism and, in instances where sensitization is very marked, localization of disease does not occur.

Exposure to maximum doses of tubercle bacilli in hypersensitive individuals results in a marked outpouring of exudate, producing destructive lesions rather than protective ones. It, therefore, seems unwise to hope for or to create early infection and disease, which even though innocuous, may allow severe sensitization with subsequent destruction.

It is our feeling that such primary infection should be withheld or prevented, if possible. It, therefore, becomes the first essential in the prophylaxis of tuberculosis to control the infecting organism.

**The Soil.**—Despite the attempts at the control of infection, which is evidenced by a marked decrease in the number of tuberculin reactors, tuberculosis

is as yet relatively ubiquitous as an infection. Not only must we, therefore, continue to prevent spread of infection, but we must render the soil innocuous, reducing hypersensitization, and thereby lessen destructive lesions in the presence of reinfection.

This latter is associated with the maintenance of good general health, as it is affected by environment, food, hygiene and fatigue, operating through the glands of internal secretion or altering the biochemistry of the body to furnish fertile ground.

**The Sputum.**—Sputum should be considered the most potent source of infection as far as human beings are concerned. Even before the discovery of the tubercle bacillus, Villemin,<sup>1</sup> in 1869, demonstrated that pulverized, dried tuberculous sputum would reproduce tuberculosis when blown into the trachea of a rabbit.

Cadaec and Mallet,<sup>2</sup> in reports in 1905 and 1907, the result of original work done since 1887, demonstrated that ordinary dust, exposed to sunlight in the ward of a hospital containing tuberculous individuals, when inoculated into rabbits and guinea-pigs by inhalation, would not produce tuberculosis, yet when such dust accumulated in dark corners, without ever being exposed to sunlight, was inoculated, some tuberculosis was found. The tubercle developed from the dust of the darkened room which had been there for some days, was diluted, due to the movement in the room; thus it required massive doses of such tubercle bacilli, contained in dust, to produce tuberculous lesions.

Cornet<sup>3</sup> in Germany succeeded in producing disease in a large number of experimental animals with dust obtained from beating rugs contaminated with dry sputum. His percentage of positive results was far greater than that of other observers.

Kuss,<sup>4</sup> in 1908, demonstrated that tuberculous sputa, dried in darkness, still contained virulent tubercle bacilli after fifteen days and that the virulence disappeared after nineteen days.

These basic experiments point the need for extreme caution in caring for all of the furnishing and bed linens, as well as the floors of the room inhabited by the tuberculous individual, if other individuals coming in contact with the patient are to be protected. Even though the patient be cautioned against covering the mouth during coughing, inadvertently at times he will fail to do so, or the kerchief he uses will be somewhat delayed in reaching the mouth, just sufficiently to allow some spray to be emitted to the area adjacent.

Great precaution should be taken as to the handling of the sputum itself. It may best be cared for by utilizing a paper bag pinned to the bedside—the patient using soft paper napkins into which to expectorate. These napkins should be dropped into the bag and ultimately consumed in an incinerator. Other devices—sputum cups, flasks and the like—are recommended and used in various institutions and such devices may be suggested, dependent upon the surroundings of the patient and his contact with other individuals from an esthetic standpoint.

The education of the patient is, therefore, important. The disinfection of the premises and furnishings of an individual having open tuberculosis for many



years formerly was practiced by attempting to fumigate such premises and their contents with lethal gas. Within recent years an abundance of sunlight and air, the washing down of walls and floors, the removal of furnishings to outdoor spaces, where direct sunlight may act to kill off the organisms, has seemed sufficient. The bedding, particularly the mattress and pillows, may require fumigation in a gas chamber or in a high-pressure sterilizer. In many instances where the mattress has been used for some time, it has been destroyed by burning. The importance of advocating and practicing cleanliness should be stressed at all times both to the patient and those in his immediate environs.

*Sputum Droplets.*—Even as dried sputum has been found to be dangerous when not exposed to sunlight for a period of hours, sputum droplets, protected by moisture and not disintegrating to allow finer distribution, have been found to be a more dangerous infecting medium.

Tappiner,<sup>5</sup> as early as 1877, demonstrated that by mixing a teaspoonful of sputum from a tuberculous individual with a pulmonary cavity in 300 to 500 c.c. of distilled water and spraying this into a cage containing a dog, subjecting the animal to one or two inhalations of one hour's duration, and repeating from twenty-four to forty-five days, twelve dogs so inoculated at autopsy were found with extensive tubercle in the lungs. Outwardly, the evidences of tuberculosis were present after the third week of spraying.

Cadaec and Mallet<sup>6</sup> had also observed that the infecting power of droplets, when inhaled, was much more effective than attempts at production of infection with dried dust. In their series of forty-five guinea-pigs made to inspire fresh, moist cultures of finely triturated sputa, all became infected.

Many other experiments have been performed in different animals by various individuals to give evidences of such infection.

In 1907 Ziesche<sup>7</sup> reported that 30 to 40 per cent. of tuberculous patients, in coughing created a spray, carrying droplets of saliva with tubercle bacilli, for a distance of forty to eighty centimeters. While the air expired by tuberculous individuals free from sputum droplets, ejected only in coughing or sneezing, has been found by different observers to be free from tubercle bacilli, this should not cause one to allow himself undue close contact or exposure.

Corper<sup>8</sup> sums this up by stating that it seems justifiable to conclude that the tubercle bacilli found in the sputum of patients with open tuberculosis (provided that the bacilli capable of artificial cultivation are a true index of the nature of those existing in the native sputum), vary only slightly in virulence in guinea-pigs and are, for practical purposes, all pathogenic; that is, in 97 per cent. of all the cases studied they will infect the child in a dose of 0.000001 mg.

The patient should be warned as to the danger of exposing others, through carelessness in the handling of sputum, as well as in coughing. The attendants should be warned to avoid the direct path of the cough, to wear an apron or gown in the presence of the patient when serving him, and to wash their hands most carefully after leaving the presence of an open case when there has been contact with any article adjacent to him.

Dishes and glasses should be kept on a separate tray, should be washed in the patient's room or bathroom—if that is limited to the patient's personal use—

and kept in his room, and the food carried to him transferred to his dishes and tray, where this is possible.

Cleveland Floyd<sup>9</sup> has demonstrated that table utensils used by the open case may occasionally harbor virulent bacilli, even after more careful washing than is customary in the average home. The water used to wash the utensils frequently contains virulent bacilli. While this may be obviated in the home by keeping separate dishes for the patient's room, the open case of tuberculosis, ambulatory, who frequents the public dining room, would seem to show the need for sterilization of dishes and utensils in such establishments.

Additional caution should be practiced where the patient is ambulant and moves about an apartment or home occupied by other individuals. Inadvertently, he may cough into his hand, open the door by grasping the knob and deposit thereon droplets containing tubercle bacilli. The next individual touching that knob may remove bacilli to his hands, and if these are not removed by washing, may find their way into the body in the taking of edibles which are picked up.

Young children, allowed to live in the same abode with ambulant tuberculous individuals, exercising their usual habit of picking things from the floor and placing them in their mouths, have become infected in this manner.

#### THE OPEN CASE.

*The Public Health Phases of Prophylaxis.*—The realization of the importance of the open case of tuberculosis in spreading infection, principally through the sputum, as detailed above, brings up for consideration the various measures which are of value in limiting the spread of infection. The detection of the tuberculous individual is of prime importance in such a campaign.

*Lay Education.*—Lay individuals should be taught to recognize the early manifestations of disease so that they will report for medical examination and supervision. Antituberculosis organizations have focused much of their attention on this problem and the vast publicity program carried on by such an organization as the National Tuberculosis Association in this country has been of considerable value in creating a tuberculosis-conscious public.

*Medical Education.*<sup>10</sup>—The practitioner of medicine, to whom the patient reports for examination when he suspects the presence of tuberculous disease, should be competent to confirm or remove that suspicion. The curricula of medical schools should contain an adequate number of hours and allow for the arrangement of sufficient instruction in the various manifestations of tuberculosis, utilizing the facilities of the medical schools, the dispensaries, the hospitals, as well as the neighboring tuberculosis sanatoria wherein intensive study of the various preventive, diagnostic and therapeutic procedures may be had. The practitioner sees the patient first, has the confidence of the patient, and when endowed with the necessary information, can have the patient adopt those measures to protect the immediate contacts, as well as the community.

Segregation of individuals having open tuberculosis should be practiced wherever possible, irrespective of whether the individual comes in contact with children or adults.

Today, as mentioned in other parts of this book, our experiences in studying tuberculosis in urban communities have created the definite thought that most tuberculosis of what is commonly termed the "adult" or "secondary" type is the result of an exogenous super- or reinfection. It is difficult to practice such segregation in the household of the individual, unless separate sleeping, bathroom and toilet facilities can be had for the patient. Where close contact results from inadequate housing facilities, hospitalization may be necessary.

In instances where the type and extent of tuberculous disease allows some form of collapse therapy to be utilized—especially unilateral tuberculosis in the caseous pneumonic group—such therapy may result in controlling the disease process so that no bacilli are extruded in the sputum. Not only is the patient thus benefited, but contact infection is obviated.

**Community Responsibility.**—Tuberculosis in a majority of instances is linked with poverty. It has become necessary for the community to appreciate the needs of such individuals, as well as to establish protective measures designed to prevent the spread of infection from open cases residing within their borders. The individual who has insufficient economic means and cannot be admitted to a sanatorium or hospital may be benefited through the bedside care rendered by the public health tuberculosis nurse. This care should include education as to the handling of sputum, the arrangement of the room and the protection of other members of the household from contact. Children in such homes should be given the benefit of open air schools, preventoria, and summer camps to promote additional resistance, engendered by outdoor living. They should be given adequate and properly selected foodstuffs to make certain of biochemical resistance.

It is of the utmost importance to continue the improvement of those occupations which have given evidence of creating a predisposition to tuberculous disease. The public must also guard against infection which can occur through the tuberculous teacher in the school room; the tuberculous nurse; or tuberculous children attending school in the same classroom with well children.

Koester<sup>11</sup> recently, in studying 994 individuals evidencing tuberculosis, was able to trace their infection, see page 22.

The danger of contact with open tuberculosis has been further emphasized by Opie and McPhedron,<sup>12</sup> who, studying a number of children under five years of age, found 80 per cent. of the contacts infected, while only 23 per cent. of the group with no known contact evidenced infection.

Barnard, Amberson and Loew,<sup>13</sup> in studying a large group of adolescents, found 86 per cent. of the contact group reacted to tuberculin, while only 67 per cent. of the non-contact group gave a positive tuberculin reaction.

Drolet,<sup>14</sup> in studying the records of 6646 children under five years of age from the hospitals of New York City, found 41 per cent. of the contact group evidencing infection and 28 per cent. of known contacts infected. This would point to the great necessity for segregation or extreme caution where segregation cannot be practiced.

**Infected Foods.**—Milk and milk products and meat have been serious offenders in the dissemination of tuberculous infection and disease.

SOURCES OF INFECTION (KOESTER).	Number	Percentage
1. Helpers or individuals frequenting open cases . . . . .	20	2 0
2. Infections in occupation . . . . .	7	0.7
3. Salesmen and employees (Common purveyors, inn-keepers, shop-keepers, etc.) . . . . .	49	4 9
4. Commercial pursuits, particularly food handlers . . . . .	49	4.9
5. Milk from tuberculous cows . . . . .	4	0.4
6. Tuberculous teacher . . . . .	197	19.7
7. Open tuberculosis in school children . . . . .	172	17 3
8. Active transmission from occupation (messenger, servants) . . . . .	0	0 0
9. Neighbors . . . . .	86	8.6
10. Frequenting other families (Sippe 5 9%) . . . . .	150	15 1
11. Contact with children from open case family . . . . .	94	9.5
12. From visiting or inviting tuberculous (open case) relatives . . . . .	41	4.2
13. From visiting with strangers with open tuberculosis . . . . .	10	1.0
14. From visiting children with open tuberculosis . . . . .	41	4 2
15. Boarding houses, hospitals, etc. . . . .	0	0 0
16. Other cases . . . . .	16	1 6
17. Indirect transmission by animals, foods, etc. . . . .	0	0.0
18. Unknown . . . . .	87	8 7
Total . . . . .	994	100 00

It was Chauveau, in his writings from 1868 to 1872, who first formulated the thought that considerable infection in tuberculosis could result from the swallowing of infected material. The tubercle bacillus in such instances gains entrance into the body through the wall of the bowel into the lymph or blood stream, localizing subsequently in one of the viscera, where it may produce disease. Other investigators confirmed these findings subsequent to the discovery of the tubercle bacillus.

Later it was shown by a group of workers, of whom Ravenel and von Behring stand out prominently, that in very young animals penetration of the intestinal wall occurred with very little difficulty and without any residual pathologic involvement in that wall.

Disse<sup>15</sup> also demonstrated that the epithelial cells of the intestine are entirely protoplasmic in the new born and that the true mucous membrane does not appear until some days after birth. Permeability of the intestinal wall is, therefore, possible within the first weeks of life without any difficulty.

Considerable progress has been made in the United States and some other countries in the supervision of foodstuffs to control possibilities of tuberculous infection.

The tuberculin testing of cows and the destruction of those found diseased, along with pasteurization of the milk, has been of considerable importance in the decrease of the incidence of many forms of extra-pulmonary tuberculosis. The rigid inspection of cattle in the slaughtering houses by the Government inspectors has also resulted in much good.

**Increasing the Resistance of Individuals to Tuberculous Infection.—**  
**Changing the Soil.**—Good health is the result of a well balanced life. An adequate amount of rest, work, or exercise; a balanced dietary and a sufficient outdoor existence, are the requisites. Our present knowledge also dictates certain rules of conduct and hygiene to prevent the occurrence of infection.

In considering the building and maintenance of resistance we find two groups of individuals: Those evidencing tuberculous infection and those who show no such evidence. While the building of resistance is important in both groups, it is doubly so in the case of the individual who shows evidence of tuberculous infection. Inasmuch as such infection may as yet be considered ubiquitous, it becomes necessary to attempt the control of sensitization, which may be marked.

*Food and Resistance.*—During the past several years, in carefully observing experiments on animals and the reactions of individuals who had been placed on certain control diets, it has become my belief that there are factors in the resistance of such individuals which are dependent upon biochemical changes incidental to such feeding. While light is gradually being thrown upon these changes, some of which we discuss under Treatment, as yet the complete mechanism of operation is not available. Much interest has been focused upon the development of serious malignant types of exudative tuberculosis in certain racial groups and upon the high mortalities suffered by these groups in the presence of such disease. The Negro, the Indian and the native born Irishman have all, in recent years, been subjects of such discussion. We take the Negro race, as an example, for study and leave out of the discussion the question of poor housing, with its congestion and inadequacy of contact protection, and pay some heed to their food habits. Rickets is known to be more prone as a disease in the Negro child than in any other race. Information from the pediatric services in our community from our large public children's hospital indicates the incidence of six cases of rickets in the Negro to one in the white child.

Rickets is a deficiency disease, produced by a calcium and phosphorus imbalance in the absence of an adequate amount of vitamin "D." It is peculiar to note that in this same community the index of tuberculosis mortality also bears the same ratio between Negro and white man of 6 to 1. I would not definitely say that these two facts are inter-related. The Negro, in the selection of his food-stuffs, has established the habit of eating, first, meat—which is chiefly pork; second, potatoes; third, such cereals as hominy, maize, grits; and fourth, lard and oleomargarine instead of butter. He takes very little milk or its products, green vegetables, eggs, red meats and those fish or fish oils which contain rich vitamins essential to health. His diet is markedly deficient in calcium and the large carbohydrate intake tends to interfere with the calcium metabolism, as pointed out in our discussion of calcium in chapter XVIII.

Is there a parallel between his dietary and his high degree of cell instability, allowing of marked hypersensitization in the presence of infection?

I have observed a lessening of hypersensitization in Negroes who were placed on a well-balanced, adequate dietary, even as similar changes have occurred in those of the white race where severe allergy or reactivity of tissue have originally been observed.

It becomes the duty of the physician to make certain that those under his care have such a balanced ration to stimulate the protective mechanism of the body. This is further discussed in chapter XVII and XVIII on Diet and Treatment, under Calcium.

I would, however, suggest that one should not lose sight of the fact that contact to open tuberculosis with frequent re-infection with virulent organisms, especially massive doses of such tubercle bacilli, may produce serious types of lesions, despite supposed resistance.

*Fresh Air.*—We consider fresh air most important in the maintenance of good health, and, even as we stress its importance in the care of the tuberculous individual, so do we stress it for the apparently healthy one.

*Fatigue.*—Fatigue, incidental to physical exertion or mental distress, may alter the resistance of individuals

Petersen,<sup>16</sup> in his work, has shown sudden changes in the calcium phosphorus ratio of the blood incidental to such emotions as joy, fear and fatigue. These are apparently induced by changes operating through the glands of internal secretion. Such changes may occur, even in the presence of what we term an adequate dietary, supplying the needs of the body, dictated by our present knowledge. It behooves one not to allow excesses of fatigue or emotional disturbances to upset the balance of health and individuals should be warned against such things.

*Prophylaxis in Childhood.*—For many years the dictum has been handed down that tuberculous infection in the first few years of life resulted in a fatality in almost every instance. The most important condition that we feel has acted for this thought is that when tuberculous infection did occur in infancy, it was usually the result of contact infection in the immediate household. With an infant clinging to and dependent upon adults in the home, intimacy of contact was more constant and prolonged. Massive dose infection with tubercle bacilli is more likely to occur under such conditions and serious disease, with death, results.

Not only do the members of the family expose infants to unnecessary infection, but kissing by strangers who assume similar prerogatives also does. Members of the family having respiratory diseases, such as chronic bronchitis and asthma, should be considered potentially tuberculous unless proved otherwise as far as contact to infants is concerned. This refers particularly to the coughing and wheezing grandparent, aunt or uncle or others who may be residents or visitors in the home of the child.

Milk-born infection is becoming more rare in this country, but, as yet, there are rural districts where tuberculin testing of cows and pasteurization of milk are not practiced. Under such conditions, when infants are artificially fed, the milk should always be brought to a boil before it is given to them. Mothers' milk may be a source of infection, resulting from a tuberculous mastitis. This pathological entity is, however, very rare. Transmission of infection in the nursing of infants may occur through indirect contact, from droplet infection, or through the most unhygienic method, which many unintelligent mothers have practiced, of moistening the nipple with saliva.

The infants of tuberculous patients should, as discussed before, be removed from any possible source of infection in the home.

The positive tuberculin reaction, indicative of an established sensitization, the result of infection with tubercle bacilli, is the most important criterion in determ-

ining the need for care in preventing actual disease when disease is not already present.

All such tuberculin reactors should have the benefit of a roentgen film examination to make certain that a disease focus has not been established. In the presence of such a focus the active treatment of the disease should be immediately pursued. Where no definite evidence of disease is demonstrable, either roentgenologically or symptomatically, the control of resistance in such reactors, especially those who have lived in contact with open tuberculosis, is the most important indication. Such children should be immediately placed on a régime allowing of good surroundings, adequate facilities for mental and physical rest, and, most important, be given a sufficient amount of calcium and vitamin D, through cod-liver oil, Viosterol, and sun exposure, as a component part of a balanced dietary.

We again stress the importance of this consideration, for having removed the child from the source of infection, it is most important to attempt to make the soil unlivable for serious disease development.

**Adequate Care of Those Convalescing From Other Diseases.**—Those factors mentioned above are to be emphasized in their exactitude during the convalescence of individuals from other diseases. Careful avoidance of contact tuberculous infection must be practiced and the upbuilding of the individual through proper surroundings, fresh air, and food, are most necessary. This is to be stressed in individuals with recurrent respiratory infections of a nontuberculous nature. It also should be most carefully heeded in the patient who has had a so-called "idiopathic pleurisy," which, as has been pointed out elsewhere, is usually tuberculous in nature. In this latter condition the patient should be maintained on a carefully supervised régime for a period of years and not of weeks.

**Acquired Artificial Immunization.**—Utilizing the thought that sensitization or allergy, developed as the result of an infection with tubercle bacilli, was important in localizing subsequent infection, a group of workers sponsored the idea of using tubercle bacilli—dead in vaccines, or alive, virulent in very small numbers, or attenuated in large numbers—in the attempt to stir up antibodies or effect sensitization and thus produce an artificial immunity. Again we reiterate that if such a produced sensitization could be controlled as to the amount of exudate which results when a re-infection takes place, or the doses and virulence of the organisms involving the re-infection could be limited, nature's protective effort might prove of avail. Unfortunately, we are not able to pass through the entire population and determine the degree of sensitization in each individual nor alter the virulence and numbers of organisms to which individuals are accidentally exposed. These considerations have created a hesitation on our part in recommending artificial implantation of either killed or live organisms in the development of sensitization. We have not as yet seen nor heard of any evidence that could point to the limitation of sensitization through such inoculation and which could guarantee definite localization of disease when re-infection, either endogenous or exogenous, took place.

**Vaccines of Dead Bacilli.**—Vaccines of dead bacilli were originally proposed by I. Strauss in 1885, Maraglino in 1903, Loeffler and Matsda in 1913, Nathan

Row in 1922, and, finally, by Langer in 1925. Vaccines of these dead bacilli were shown capable of stirring up tissue reactions which resulted in actual tubercle formation and, in some instances, in active tubercle formation with caseation. The tendency was for these areas of reaction to form encysting walls of fibrosis, or to become resorbed so that only temporary sensitization occurred through their use. Any supposed benefits were limited to a very short interval of time.

*Vaccination with Live Tubercle Bacilli.*—A group of individuals, of whom Koch, Webb, Gilbert and von Behring may be mentioned, have attempted to develop immunity in tuberculosis through inoculation with virulent living tubercle bacilli. Webb and his associates even developed an apparatus and technic to isolate single tubercle bacilli for inoculation purposes. The aims of these men were discontinued because of the great danger in causing tuberculous disease from such inoculation.

Calmette and his associate, Guerin, following the classical researches of a group of individuals prominent in this field of tuberculosis endeavor, about three decades ago, began experimentation to produce immunity through the injection of living tubercle bacilli. Their researches gradually extended to the development of an attenuated virus, which, after many years of growth, apparently seemed devoid of any virulent characteristics.

After a number of years of experimentation in animal inoculation, the method has been extended to one of vaccination; first, to newly born infants in contact with tuberculous mothers, through the oral feeding of vaccine in definite amounts to such infants. Subsequently, children at later years were given the vaccine and at the present time its use is extended to children of all ages, as well as some adults who evidence negative sensitivity, as determined by tuberculin reactions.

In addition to the oral route, at the instance of several workers, the vaccine is now introduced intra and subcutaneously, especially at the older ages. By this latter method a greater efficiency is claimed by the workers utilizing it.

The immunologic considerations of this method have been further discussed by Mellon and Koch in the chapter on that condition.

Approximately 2,000,000 individuals, mostly children, have received inoculation with BCG. Much controversy as to its value continues.

**Marital Tuberculosis.**—The marriage of a tuberculous individual brings up several problems: (1) Increased physical burdens; (2) increased economic burdens; (3) dangers associated with the marital state; (4) dangers of pregnancy, childbirth to the female patient; and danger to the possible offspring; (5) and the dangers of contact infection to the unaffected consort.

The increased physical and economic strain, as well as the physical strain encountered in marital life, may be factors in altering resistance and may prevent healing or allowing extension of disease. Marriage of the tuberculous should be avoided because of these conditions. Where a tuberculous individual has married, contraception should be practiced until certain healing has occurred. The gravity of pregnancy occurring in the tuberculous has acquired a different outlook within the past several years. Falls discusses this matter in great detail



in chapter XL. Infection of the offspring is always a potential danger and the child born of a tuberculous parent with active disease should immediately be separated from its mother until definite certainty exists that she has not an open tuberculosis. In the presence of an open tuberculosis in the father, similar steps must be taken to protect the infant.

As to the danger of transmitting disease to the consort who has no evidence of tuberculous disease, the idea for some time has been that little danger exists among married people.

Opie and McPhedron,<sup>17</sup> in making a study of 533 married couples, over a varying period of time up to eight years, conclude that husbands and wives in marital contact with tuberculosis, under varying conditions, are infected from five to nine times as often as persons with no known contact with the disease. Husbands are infected oftener than wives. The frequency of infection in wives exposed to husbands with tubercle bacilli in the sputum is 35.5 per cent.; in those exposed to husbands with no demonstrable tubercle bacilli, 22.9 per cent. The incidence of infection in husbands exposed to wives with open tuberculosis is 45.6 per cent., and when there are no tubercle bacilli in the sputum, it is 35.9 per cent. These studies involved careful physical, as well as roentgen, examinations.

This high incidence would indicate that marital life produces no immunity from the dangers of an intimate contact with open tuberculosis, even in adult life, and that precautions must and should be taken to prevent such infection.

**Tuberculosis and Physicians and Nurses.**—Caution should be observed among physicians and nurses who are in constant contact with tuberculous individuals. The low incidence of development of tuberculosis in medical men and nurses, and in attendants in tuberculosis institutions is due to the regularity of living, as well as to the knowledge that tuberculous patients, capable of transmitting infection, are present, and precautions to definitely control such infection are constantly carried on. There should be no let-down in the vigilance observed by those attending tuberculous individuals. Medical men and nurses should seek to be examples of proper conduct in preventing infection and proper living in maintaining resistance against disease.

**The General Hospital in the Care of the Tuberculous.**—For some years<sup>18</sup> we have fostered and promulgated the idea of utilizing certain divisions of general hospitals for the care of the tuberculous in studying (1) the suspect case for diagnosis; (2) the case for whom surgery of the chest or other organs is indicated; (3) the patient who awaits admission to a sanatorium and who should be removed from intimate contact in his home; and (4) the patient for whom no sanatorium facilities are available.

There is no reason, granted proper conditions and proper management exist, why the tuberculous patient cannot be cared for in the hospital. Under improper conditions and poor management such a course is definitely inadvisable and even dangerous. The admission of open cases of tuberculosis to the rather crowded environment of a large general ward should not be allowed. Patients debilitated from other chronic conditions should not be subjected to the pos-

sibility of tuberculous infection. This possibility must be absolutely and finally ruled out before we can even dare to consider the proposition, yet suitable arrangement and cautious supervision and management will eliminate even a remote possibility of "house" infection.

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## CHAPTER XIV.

# HOME TREATMENT OF TUBERCULOSIS.

BENJAMIN GOLDBERG

Estimates in the beginning of the year of 1934 indicated that there were approximately 600,000 individuals with active tuberculosis in the United States at that time. The various institutions which function in caring for tuberculous individuals had a sum total of 76,000 beds in which such individuals could be treated. This includes private as well as governmental institutions. With all these beds filled there would still remain approximately 525,000 individuals who at that specific time must be given treatment for their tuberculous disease in their homes.

This places the burden of medical supervision upon the practicing physician, whether he gives such service in his private practice, or through the medium of some dispensary clinic. These statistics clearly indicate the very great importance of home treatment. Furthermore they indicate that the sanatorium is in most instances an adjunct to home treatment, rather than that home treatment is an adjunct to the sanatorium.

It should be emphasized that a period of residence in a tuberculosis institution, properly equipped and conducted, is desirable in the application of surgical procedure, to aid in obtaining a sufficient mechanical control of the pulmonary tuberculous process, or to allow of the treatment of a serious complication.

## ECONOMIC FACTORS.

The economic factor deserves first consideration. Tuberculosis is usually a chronic disease entailing physical disability of long duration. This disability, in turn, except in cases of fortunate individuals, carries with it varying degrees of financial embarrassment. The degree of financial embarrassment in many instances determines the nature and the character of the home treatment possible. From the point of view of economics, families of individuals considered for home treatment may be classified as:

1. **The destitute poor** in which the wage earner is stricken and in which the family must be supported by charity. Home treatment in these cases is subject to very definite limitations. Individuals in this category should be institutionalized wherever possible.

2. **The Family of Moderate Means.**—The patient may not be able to afford care in a private sanatorium, but may remain at home without working, and take the cure satisfactorily. As a rule the housing, hygienic and dietetic factors are favorable in this group and proportionately encouraging results may be expected.

3. **The Wealthy or Financially Independent Family.**—The patient may not choose to enter a sanatorium, desiring the personal comforts that only the

home environment affords with the individualistic supervision of his personal physician. This type of fortunate individual, if he can subject himself to the necessary régime, has no need for sanatorium treatment, and may find or develop all the advantages of sanatorium care in his own home.

In my personal experience, patients under supervision in their own homes, with meticulous care, have yielded excellent results in treatment of this disease. Each individual case should be considered a problem in itself. The family physician will have to decide how to accomplish the utmost with the facilities at his command. He must subject every individual case to a refined economic analysis, and must govern the supervision of the patient so as not to impose financial burdens that the family is unable to bear. It is both cruel and useless to prescribe a dietetic or hygienic régime that is beyond the financial reach of the patient.

If the doctor prescribes the most expensive cuts of meat and an elaborate sleeping porch, the patient will become dissatisfied with his round steak and humble lean-to, and will not make satisfactory progress. The doctor must "cut the coat according to the cloth." He must not demand impossible conditions of the patient and must not portray the cure of tuberculosis as something to be reached along certain ideal routes and along these alone.

**Preliminaries.**—The home treatment of tuberculosis should not be lightly undertaken. The physician at the outset, should outline in a most careful and definite fashion, every phase of the treatment, detailing information to the patient and his family so that their education will be sufficient. The physician having gained the confidence of those involved must next determine that the arrangements in the home are such as will not make any interference with the treatment possible. All business and household responsibilities must be deleted from the life of the patient. Any other factors which might tend to disturb the rest of the patient should be corrected, to allow of the necessary mental and physical quietude.

The physician should personally inspect the home, select the room, determine the furnishings which are to remain and suggest the changes that must be made.

### HOME ENVIRONMENT.

**The Patient's Abode.**—The patient should be given the airiest, sunniest, and most pleasant room in the house. It should, if possible, be a corner room with more than one window, and preferably a southwest exposure. The furnishing should be simple and cheerful and not glaring or obtrusive. Only such draperies, furniture and wall decorations should be allowed as are necessary to lend tone to the room and do away with its bareness. The floor should have one or two small rugs to impart a sense of warmth. Curtains, washable drapes or a few favorite pictures sometimes add to the mental quietude of the patient.

If the room is sufficiently large, and the patient is on absolute bed rest, twin beds can be utilized, and the patient shifted from one to the other. This prevents postural fatigue. A chaise lounge or reclining chair of proper con-

struction, may take the place of the second bed, and be utilized while the bed slept in is being freshened at intervals during the day.

A back rest is a welcome addition in shifting the posture of the patient. An electric light switch and hand bell within easy reach of the patient's hand are appreciated conveniences.

The windows should be arranged so that they can be opened easily at the top or bottom both day and night. The patient should be protected from drafts by means of deflectors, ventilators and screens, many types of which are on the market.

In some instances a sleeping porch is impractical or unobtainable. The room should then be so arranged that the patient may have as far as possible the advantages of outdoor sleeping through good ventilation.

*Outdoor Sleeping.*—A room connected with a porch is the ideal arrangement for outdoor sleeping. In many homes this arrangement makes possible the moving of the bed into a room in the morning for bath, toilet and general care of the patient, or when the weather is too severe. Open porches may be fitted up and enclosed with French windows or canvas curtains. The comfort of the patient is most important and attention to detail is the keynote of success. Additional accessories such as a bedside table, and a book rack may add to the comfort of the patient.

*Bedding.*—For those in moderate circumstances an iron cot six feet by thirty inches, with a spring cover may be utilized. In cold weather the spring of the bed should be covered with felt roofing paper sewed to the edges to prevent the wind from coming in from below. A felt mattress, at least three woolen blankets, plus a cotton blanket to sleep between, and a khaki cover may be considered ordinary equipment.

*Dry Bed Clothes* are of considerable importance and additional bed clothes should be kept in an adjoining room to allow changing in the presence of dampness, and for patients who are subject to night sweats. Only sufficient bed clothes to maintain body comfort should be used. An excess or the lack of bed clothes may produce discomfort, preventing restful sleep.

*The Sleeping Bag.*—Several types of sleeping bags are on the market which are suitable, under certain conditions and limitations, for outdoor sleeping. In cases in which, for one reason or another, the patient must get along with comparatively little attention, a good type of sleeping bag is preferable. Unless the patient has an attendant or relative to make his bed in a competent and efficient fashion, he will not rest comfortably. The sleeping bag is easily manipulated and will meet the indications of the case just mentioned. Its disadvantage, however, is that it is often difficult to keep clean and unless precaution is exercised may become insanitary. For extreme cold weather the Arctic Eiderdown Sleeping Robe is comfortable and convenient.

*Sleeping Out and Sleep.*—Sleeping out is not by any means beneficial for every type of patient and in all kinds of weather. In the first place, as already stated, the home conditions and the type of porch may be such that comfortable outdoor sleeping is out of the question. In other cases, the physical condition of the patient may indicate outdoor sleeping. Precaution should be taken to protect

the patient as far as possible from disturbing or nerve-racking noises. The porch should be so constructed and located as to minimize noise and should be sufficiently protected to shelter the patient against high winds and driving rain storms. The patient should be able to sleep comfortably under all weather conditions. Not all patients may be suited for outdoor sleeping at all times. Owing to such conditions as heart disease, low blood pressure, severe anemias, bronchitis, sinus disease, etc., the patient's physician may advise temporarily or even permanently against "sleeping out."

Sound, refreshing, unbroken sleep is one of the most vital considerations in the cure of tuberculosis. Inasmuch as rest is the prime consideration in this treatment, the value of restful sleep cannot be over-emphasized.

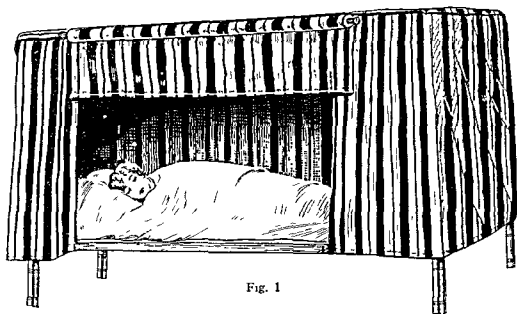


Fig. 1

*The Porch Tent*—The porch tent pictured above was devised by one of my patients. It is considered one of the cheapest, most comfortable and best arranged of the outdoor sleeping equipments.

The wooden framework, made of 1 x 2 inch pine, costing at any lumber yard about 50 cents, is built up around a standard cot on all but one side, which side has a large roller curtain four feet in length, which can be raised or lowered as weather conditions indicate.

*Clothing for Outdoor Sleeping*—There has been a tendency to over-clothe the patient. His fear of cold often induces him to wear exceedingly heavy woolen underwear, chest protectors, mufflers and other similar articles of clothing. The patient should be warm and comfortable, but should not be overheated and should not perspire on the least exertion.

The patient should be told that he must get along on the least amount of clothing with which he feels perfectly comfortable. In the writer's experience for this climate, medium or, better still, light woolen underwear next to the skin is the material of preference. The underwear should not fit too tightly

and the lightness of the material may be counterbalanced by adding heavier outer garments as indicated. At night the patient should change to a similar suit of light woolen underwear, and in the cold weather wear over this a comfortable suit of flannel pyjamas.

Owing to the disturbances of circulation common in tuberculosis the extremities need special attention. Cold hands and feet are frequently complained of, and this condition must be met if the outdoor regime is to be a success. Woolen mittens and woolen socks of the desired weight should be worn. Friction and frequent changing of the socks is sometimes beneficial. Eiderdown leggings or boots are sometimes advisable. The llama wool garments, combination suits with hood, gloves and stockings attached, may solve the problem in certain instances. A hood, helmet or woolen toque is often worn on the head. Chilling of the nose, particularly in the early morning hours, may be uncomfortable and cause insomnia. The wearing of a woolen lined mask will meet this objection. Some patients apply cold cream to the face at night and claim that this procedure helps to retain the warmth.

For sitting out during the day, a heavy overcoat, preferably a fur coat is indispensable in this climate. For the long hours in the reclining chair, extra wraps are needed.

*Open Air Versus Good Ventilation.*—Fresh air is one of the prime principles in the treatment of tuberculosis.

The patient, to enjoy the full benefits of fresh air, must either be out in the open twenty-four hours each day, or else during such time as he is indoors, must live in a room having constant circulation of pure air from the outside. The comfort of the patient, however, is not to be neglected. In severe weather, exposure should not be permitted in the case of the feeble or far advanced tuberculous, who are not tolerant. Rest indoors in a well-ventilated room is preferable to a sleepless night out of doors. There is danger in stagnant air only insofar as the increased temperature and humidity in the poorly ventilated room tends to increase the irritability of the patient, make him more uncomfortable and prevent adequate rest.

\* In many instances the belief that night air is harmful is still abroad and calls for explanation. The subject may be disposed of in one terse sentence: "The only night air that is bad is the air of the night before; open your windows and let it out."

Cool air, not cold air, is to be desired. Cool air is restful; stimulates the tissues to increased vigor, counteracts anorexia and lends tone to the general body condition. The tuberculous patient always improves at the best rate in a cool atmosphere.

*Home Sanitation*—The dishes and eating utensils should be kept separate. The patient should be liberally supplied with paper napkins and the attendant or relative should see that the patient always covers his mouth when coughing or sneezing, and deposits the napkins in a paper bag pinned to the head of the bed, which bag with its contents is later burned. If a sputum cup is used, it should consist of a metal container with a paper cup filler which may be removed and burned at will.

The bed linens and towels used by the patient should be kept separate, and should be boiled, preferably in a separate container. The room should never be dry-swept or dusted. It should be mopped with water or with an oil mop and should be dusted with an oiled or moist rag.

Particular attention should be paid to dark corners and corridors, as in such places the tubercle bacillus is likely to remain virulent for a long time.

The ambulatory patient should be carefully instructed not to use his bare hand to protect a cough. He should be warned against the possibilities of transmitting infection on door knobs and other such means.

When the patient leaves the home the rooms which he occupied either temporarily or permanently should be thoroughly cleaned. Soap and water and plenty of scrubbing are preferred. The walls should be washed down, the windows should remain open and the room given as much direct sunlight as is possible. Articles of clothing, rugs, soiled bedding that cannot be disinfected, should be destroyed.

### PERSONAL HYGIENE.

**The Bath.**—The bath should be tepid rather than warm and should be taken in the evening before retiring. A bath at this time tends to induce restful sleep. Such a bath should be taken at least three times a week. Tuberculous individuals, unless otherwise advised by the physician, should practice sponging the chest. The sponge should be taken with tepid water at first; water of a lower temperature should be used as the patient becomes accustomed to it. The sponging should be followed by a brisk rub with a turkish towel; the ultimate result of this procedure is a ruddy, dry, skin and a sense of comfort and well-being. This sponging tends to increase the resistance of the patient to temperature changes and always has a stimulating and invigorating effect.

Patients who have been in the habit of taking cold baths before their illness and who get favorable reactions may continue to do so, on the advice of their physician. Many patients, however, do not bear the complete cold bath well, they chill, the extremities become livid and they feel cold and depressed for a considerable time afterward. For such patients the cold bath is injurious and injudicious.

**The Teeth.**—The teeth must be brushed morning and evening, using a good dental cream, followed by a mouth wash. The mouth wash should be cleansing and soothing to the taste. This will clear the mouth and throat of accumulated mucus.

**Smoking.**—Smoking in moderation may be practiced in the open air. It should never be permitted in the room of the tuberculous patient, nor should the patient be allowed to inhale smoke. Cigar or cigarette smokers should use a long holder. The chewing of tobacco, with its consequent mouth and throat irritation, should not be permitted.



## CHAPTER XV.

# NON-SURGICAL REST, EXERCISE AND OCCUPATION

BENJAMIN GOLDBERG.

Rest is the most important single factor in the treatment of pulmonary tuberculosis. Realization of its importance was first emphasized by Detweiler, pupil and protege of Brehmer, German pioneer of sanatorium therapy.

The lungs are vital organs and respiration is a vital function. Considering the average respiratory rate as 17 per minute, the lungs should contract and expand over 28,000 times in the period of 24 hours. In the presence of disease with increased metabolic activity, this rate, would of necessity show a definite increase.

*The physiology of respiration may be summarized so as to determine how rest may best be applied on a non-surgical basis. The mechanism of inspiration functions as a result of two conditions. The contraction of the diaphragm draws the central tendon of the diaphragm downward and enlarges the thoracic cavity in the vertical diameter. At the same time an increase in the thoracic cavity around the periphery of the diaphragm is caused by the flattening of the muscular dome or arch; in addition an increased intra-abdominal tension is developed. At the same time during inspiration the ribs which normally slant downward are elevated through the contraction of the various muscles of inspiration. These changes result in an expansion of the lungs which is indirectly proportionate to the increased enlargement of the chest cavity.*

Once the bony and muscular framework have acted to enlarge the thoracic cavity, the negative intra-thoracic pressure aids in a more complete expansion of the lungs.

Diminution in the size of the thoracic cavity is obtained by contracting the abdominal muscles and forcing the diaphragm upward. Thus, with the contraction of the internal intercostal muscles and the several accessory groups through depressing the ribs, aids in the diminution of the lung capacity.

Quiet breathing in man is usually diaphragmatic or abdominal. The costal type of breathing causes greater lung expansion.

Respiration is also affected by the action of an increased blood  $\text{CO}_2$  content, as well as an increased blood  $\text{pH}$ , acting on the respiratory center in the medulla. These blood changes may occur not only through increased physical activity with its increased metabolism, but through mental or psychologic reactions affecting the secretory mechanism of the body.

Both physical and mental rest are therefore important in curtailing body metabolism; thus tissue requirements for oxygen and gaseous interchange are lessened and respiratory undulation is diminished. The decrease in the rate of respiration, its depth and its force exercises a beneficial influence on inflammatory lesions in the lungs. It diminishes the massage created by pulmonary movement

and the spread of local inflammatory material through the bronchi and lymphatics. This decreases the absorption of toxins into the circulation. The passive congestion incidental to pulmonary relaxation stimulates granulation tissue formation, which further aids in walling off the disease process.

**Methods of Obtaining Rest.**—Nature has not supplied pulmonary tissue with a sensory nerve distribution as other tissues throughout the body have been. Consequently, the lungs when invaded by inflammatory processes do not directly react with pain, to inform us of this invasion. Neither is there in pulmonary tissue a muscular element to cause contraction and natural immobilization as is noted in local inflammation in other parts of the body. Therefore, in pulmonary disease comparative rest or immobilization is secured by:

1. Limiting diaphragmatic activity.
2. Curtailing costal breathing.
3. Lessening the body metabolism

These may occur through:

1. Voluntary body and mental rest on the part of the patient with the accompanying relative rest of the pulmonary tissue.

2. Associated pathological processes such as pleurisy with adhesions.

3. Artificial means:

Non-surgical in the application of various splints, casts and appliances to the chest wall.

Surgical procedures such as pneumothorax, phrenicectomy, apicolysis and thoracoplasty.

Non-surgical pulmonary rest is relative and never absolute. We therefore term it "general rest."

The patient who is ill with active tuberculosis should be on general rest. By "general" we mean a complete relaxation of the body musculature and at the same time a relaxation of all mental processes. The patient on general rest remains in bed twenty-four hours each day. He does not get up for meals or to use the toilet, and all body motion should be restricted while in bed as much as is possible.

General rest should always be insisted upon at the onset of treatment, irrespective of the condition of the patient. This is ordered to determine the reaction to such rest, and to the treatment in general. Many patients have been seen who were afebrile while ambulatory, and yet on full rest in bed immediately manifest a fever.

A great many tuberculous patients at the onset of treatment find it difficult to coöperate in the matter of rest. It is difficult for high strung tuberculous individuals to learn relaxation and practice it immediately. Some say that they are not sick enough to remain in bed constantly, others that continuous bed rest weakens them. They want to be up and around at least part of the time. It requires tactful perseverance, often insistence, coercion and joviality to tide them over the first days of general rest. At the end of the second or third week, the benefits accruing from such routine are usually seen, and the patient becomes more amenable to suggestion.

*Progressive Relaxation.*—Edmund Jacobson<sup>1</sup> has developed a method to cultivate thorough-going rest in man. It is called progressive relaxation. When limited to a part, as the chest, it is called *local*; when it includes practically the entire body, lying down, it is called *general*. Another type is called *differential relaxation*. By this is meant the utmost in economy of muscular effort during action, so that what is accomplished by the individual in his daily life involves the least strain on the organs.

There is evidence that the average person does not know when he is tense and that he can profitably be taught to recognize the locality of muscular tenseness, thereby aiding him to relax.

During an acute spell of nervousness, the physician will counteract the symptoms if he induces the patient to relax completely. Simple instructions to this effect may suffice or he may be obliged to show the patient something about relaxing the particular muscle groups that seem tense. But for chronic fatigue or for chronic nervousness, nothing short of systematic training to relax the entire muscular system is required.

The patient is taught, one by one to relax all of the noteworthy muscle groups of the entire body. As he relaxes a given part he simultaneously relaxes all parts that have previously received practice. He finds that relaxation is an art which has to be acquired by daily practice, just as a language must be learned or some act of skill such as playing billiards.

Most commonly patients complain that when they lie down "their minds keep on working" or "that they cannot stop thinking." In order to handle such difficulties, the physician needs to know something about physiology of mental activities. Recently it has been found by electrical methods that during any act of thinking or emotion, there always occurs tension in some specific muscular locality. Patients can readily be taught to discover these localities for themselves and to relax the muscles involved. There follows a mental quiescence which is one of the aims of treatment in tuberculosis.

Differential relaxation is a direct means to avoid the nervous excitement and unrest, which, as physicians agree, are inimical to the welfare of the tuberculous patient.

Non-surgical rest as previously stated is relative; not absolute, but in properly selected patients the following additional methods have been of value:

*Silence.*—Talking increases respiratory undulation and I ask my patients to practice silence or quiet whispering to relieve the body of such effort.

Schaeffer<sup>2</sup> has emphasized this method, "the silent bed cure" to be utilized where proper progress toward recovery is not forthcoming, but inasmuch as it is beneficial, I recommend it to all patients.

*Controlled Diaphragmatic Breathing.*—Quiet, shallow and slow breathing may be taught the patient who has not an extensive destruction of alveolar tissue with the resultant anoxemia from that cause.

Knopf<sup>3</sup> first discussed this under "Controlled Diaphragmatic Breathing." During such breathing respiratory function is carried on almost entirely at the base of the lung, and respiration can be curtailed to an average of ten per minute in many cases. Associated with this, the patient feels a peculiar sense of quietude

and relaxation. After it has been practiced for several days it becomes almost automatic.

*Postural Treatment.*—Placing the patient on his diseased side, the postural treatment recommended by Webb,<sup>4</sup> Forster and Houck, is of value in controlling expansion of the lung on that side. They further recommend the use of a small rolled pillow under the chest to aid in compressing the chest wall.

Shot bags to weigh down the chest have also been advocated in conjunction with such postural rest to add further compression. They weigh approximately one to two pounds.

Gekler and Weigel<sup>5</sup> amplify this method, utilizing a special mattress pillow three inches high and stuffed with two pounds of hair. It is twenty inches long and has side walls, and when placed under the patient lifts the shoulder from the bed so that pressure is directly had against the ribs. This is utilized for one hour the first day, increased one-half hour daily until the patient devotes sixteen to twenty hours out of the twenty-four in such posture.

There may be a temporary increase of cough and sputum during the first week, which subsides thereafter.

In bilateral tuberculosis where artificial pneumothorax has been induced on one side, postural treatment may be of value on the other.

*Compression Belts and Bandages*—Belts of various types have been built, developed and used to limit respiratory excursion in pulmonary tuberculosis. Sewall and Sweezy utilized a constricting elastic band three to three and one-half inches wide, which was tightly wound around the chest, fitting as high as the axillæ would permit.

Beasley,<sup>6</sup> utilizing a mole skin belt padded with curled hair, encircles the lower chest with it from the costal margin upward. This belt is five inches wide and is tightened by a lace, such as used in a corset.

*Lung Splint.*—Wingfield,<sup>7</sup> for unilateral or bilateral apical lesions, has developed an aluminum shoulder piece, covered with rubber and lined by a rubber pneumatic bag, which can be inflated to any desired pressure. It exerts an inward pressure in all directions, the power being derived from its own rigidity and anchorage to the other shoulder and thigh. This does not interfere with the function of the other lung. The entire splint and accessories weigh about one to one and a half pounds.

*Plaster Cast.*—A plaster cast in the treatment of pulmonary tuberculosis was applied in a series of cases by Levitt,<sup>8</sup> and is used occasionally by others. The cast is applied during complete expiration. It is kept on for a period of two to four months and results in improvements in the usual manifestation of toxemia and bronchial irritation.

Personally, I utilize non-surgical rest in those instances where the disease process is of an exudative or exudative-productive type, or where the patient with a caseous pneumonic tuberculous disease refuses the indicated type of surgical intervention.

Under a carefully supervised régime, special mechanical appliances have been found unnecessary in accomplishing rest. My patients are always placed on

silence, taught low diaphragmatic breathing, where that is possible, and given whatever benefits may accrue from postural compression.

*Rest and Exercise.*—Exercise is allowed a patient with pulmonary tuberculosis when evidence of tuberculo-toxemia, as manifested by fever, tachycardia and anorexia, has abated or when cough is not a prominent symptom, and in the absence of hemorrhage. It has been my rule to keep every patient observed with an active tuberculosis on a minimum of six weeks of general rest, irrespective of the subsidence of such tuberculo-toxemia. It is far wiser to err on the side of a continuance of rest than to allow the patient to exercise too early in the course of the disease.

The proportion of rest and exercise should vary not only with the patient, but with the type of disease and the general conditions manifested by each individual. In addition to a cessation of the symptoms of tuberculo-toxemia, as mentioned above, I believe in the utilization routinely of a new roentgen film study, which should evidence a regression of the lesion, corroborating the subsidence of the toxemic manifestations. In addition, the physical examination should also show a diminution of physical findings, although this latter is not nearly as accurate a guide as are symptoms and roentgen findings.

Rest and exercise must be considered as medicaments to be prescribed by the physician, to be regulated by him and to be taken in proper proportion only under his instruction and supervision.

Patients having the acute benign types of tuberculosis and patients with the chronic infiltrative types, tending as they do to an earlier decrease in the toxemic symptoms, can be allotted exercise with greater safety than those of the caseous pneumonic groups where the disease tends to extend because of increased physical exertion.

The stage of preliminary exercise is of importance. It is the transient stage between absolute general rest and graduated exercise. At the end of a period of six weeks of absolute general rest, with temperature and the pulse remaining at a normal level for a period of days and the roentgen findings, as indicated above, showing improvement, the patient is allowed to discontinue such absolute general rest. At first he may be allowed to sit up in bed for one-half hour or an hour. This may be increased each day by fifteen minutes until, at the end of a week, he may be allowed to sit in a reclining chair for a stated period each day. As the tolerance to such posture improves, he may sit up for one meal a day, then two meals, and finally for all meals. Even in this transitory stage the patient should be carefully observed for the effects on the pulse and the temperature. Fatigue should never be allowed. It is damaging to the patient and once it has occurred the patient has exceeded his tolerance and begins to break it down. Consequently, when instructing a patient, he should be warned never to exercise beyond the point of first evidences of fatigue, but should cease immediately and rest when such evidence appears.

*Graduated Exercise.*—Graduated exercise aims at the increase of physical resistance by exercise of various types taken in gradually increased doses. Improvement in the physical status of the patient is, of course, an important objective in the treatment. The gradual increase in the exercise results at the end

of a period of months in an individual somewhat physically hardened who graduates from his exercise as prescribed to a similar number of hours of exercise at some form of employment, rendering a pecuniary return. Without such exercise we are likely to have a soft, flabby, fattened individual, unable to work and subject to relapse when he attempts work which results in intense fatigue. Graduated exercise is of various types, depending upon the surroundings of the patient. It should not be commenced until the patient is able to dress himself and be up and around a considerable portion of the day, as discussed in preliminary exercise, without inconvenience, discomfort or injury.

*Walking*, as a graduated exercise, was described with considerable detail by Marcus Patterson of Frimly, England. He arranged a walking schedule as follows:

1. Walking in the open on a level grade one-quarter of a mile a day for the first week.
2. One-half a mile a day for the second week.
3. Two miles a day for the third week.
4. Four miles a day for the fourth week. (At the end of the fourth week the patients, in addition to their walking exercise, can clean up their own rooms, make their own beds, etc.)
5. Six miles a day for the fifth week

Walking develops the muscular tone of the lower portion of the body. The upper portion of the body must be developed by different methods. Those established by Patterson consisted of six grades of outdoor work to follow the various grades in walking. The outdoor work starts with the carrying of a basket containing ten pounds of dirt from one spot to another. The weight is increased gradually up to a maximum tolerance. This latter may not be feasible in the home and there it may be replaced by light gardening or by slow upper body calisthenics.

*Precautions.*—Under such exercise routine as indicated above the physical condition can, under close supervision, be markedly improved. One must be very careful that patients in their early grades are on absolute general rest between their exercise periods. It is only in this way that the toxemia which tends to be created can be controlled. The symptoms of toxemia which tend to call for a diminution in the exercise schedule are:

1. Loss of appetite.
2. A rise in temperature above 99° Fahrenheit, which often is accompanied with languor, headache, loss of appetite and generalized pains and aches.
3. A tachycardia or an increase in the pulse rate above 100, which tends to persist. This latter manifestation is a most important one and should be carefully observed.
4. An increase in cough or in the amount of sputum brought up.
5. Loss in weight, which tends to continue, associated with mild toxic manifestations.

*Outdoor games and other forms of diversion* may be encouraged once a tolerance for a moderate amount of exertion has been developed. These should not be too exerting, especially in the stretching of the chest through un-

necessary deep respiratory motions, nor should they allow of any acute or gradual fatigue. During the period of later convalescence fishing, croquet, slow bicycle riding and playing on a putting green of a golf course are examples of what may be done.

*Occupation.*—The future occupation for the convalescent patient is a problem that requires concentration. Everything else being equal, the industry or occupation in which the patient can receive the greatest compensation, working the fewest hours, is to be preferred. It is for this reason that vocational training or training the patient for certain light trades or occupations is, in many instances, productive of excellent results. Such occupations as telegraphy, commercial art, stenography, sewing, embroidery and beauty culture are examples of those which can be controlled to minimize the physical demand made upon the patient, so that the individual without a trade, who otherwise would have to do laboring or heavy household work for a living, goes along much better in such new occupations.

Demonstration projects to prove the feasibility of such work have been shown in the Altro work shops of New York City, the Livingston Press at the Potts Memorial Hospital in Columbia County, New York, the Printing and Bookbinding shops of the J. C. R. S. Sanatorium at Spivak, Colorado.

For the patient who already has an occupation which is not unusually hazardous or laborious, considerable thought should be taken before a change is advised. Thus, even though recent surveys, according to Burhoe, indicate only 38 per cent. of patients as being desirous of returning to their previous work, we regard it as a safer principle to try to return the individual to the position in which he can capitalize the knowledge, skill and experience he has already gained. It is much easier for the patient past his youth to traverse the road he has already traveled than to break new paths for himself in other directions. Unless then the patient can materially shorten his hours and lighten his labor, without at the same time curtailing his weekly remuneration too much, he should be encouraged to return to his old occupation, making certain of a proper environment.

As already stated, for the patient who has no trade or occupation, and who will have to resort to labor, nothing can be lost by trying to gain his livelihood in a less arduous manner. Individualization is the answer to this problem. The capabilities, initiative, mentality and characteristics of each patient should be studied individually by a competent and interested physician for the betterment of that patient.

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## CHAPTER XVI.

### DIET.

BENJAMIN GOLDBERG

#### GENERAL CONSIDERATIONS.

Food is a basic factor in the recovery of the tuberculous individual. The patient who has access to good food carefully selected and properly cooked, who has a good appetite and a physiologically sound gastrointestinal tract, has at the onset considerable in his favor. Unfortunately, this Utopian picture is only infrequently found.

The toxemia produced by this disease, with its increased metabolic activity plus anorexia and frequent digestive upsets, results in a loss of weight, which in extreme cases becomes emaciation. This is especially true in many instances where the patient and his family are poverty stricken. Fortunately, most communities are now socially minded and so organized that aid is forthcoming to these sick poor. Within reason, the patient in the family of moderate financial means can have the food he requires.

Three well balanced meals a day, given at regular dining periods, are the basis for the dietetic treatment of tuberculosis. The food should be of the kind the patient likes or is accustomed to, of good quality and a little more in quantity than the average healthy individual of similar physique would take. In some homes it may be necessary to emphasize the importance of the preparation and cooking of the food. It has frequently been noted that many housewives and housekeepers fall into the habits of easy cooking. They develop a routine of turning out a few dishes that are easy of preparation and are content to rest on these laurels. In many instances the same dishes are prepared day after day, cooked in the same fashion, which only too frequently is a very poor fashion. Such individuals have not been taught nor have they attempted to explore the region beyond the threshold of culinary art.

The proper cooking of vegetables is especially essential, and in this branch of cookery the average housewife is frequently deficient. This improper cooking of vegetables is not limited to the preparation of food in the homes of the poor. The cook or housewife usually places her vegetables into a pan full of water, boils them for a considerable period of time, draws off the water and throws it away. She thus removes the mineral salts and some other desirable constituents so often important in effecting the proper body chemistry. To cook vegetables properly very little water should be used, in fact just sufficient to cover them. The water should be allowed gradually to boil away so that when cooked the vegetables have no excess fluid. Better still, the vegetables may be cooked in one of the various types of "steamers" in which no water at all is used, except that contained within the vegetables. The vegetables in one of these utensils are cooked over a slow fire, simmer in their own juices, and both the aroma and mineral salts are preserved.



Additional nourishment between meals becomes a habit in the feeding of many patients. The members of the family as well as the patient believe that he should be constantly nourished. The result is that the extra lunches very frequently interfere with the appetite at regular meal times. The gastrointestinal tract, like any other organ, needs rest and cannot be expected to function efficiently, if it is continually to carry this burden. Forced feeding under such conditions, even in the presence of a gain in weight, may result in gastroenteritis, with the consequent rapid loss in weight which at times is very disturbing. However, if the patient is malnourished and below weight, an added bit of nourishment in the form of milk, egg-nog, or malted milk between meals may be given, providing they do not tend to cause digestive disturbance, or upset the appetite and cause a limitation in the amount of food taken at regular meal-time.

The food habits of different races vary enormously as is seen in geographically widely separated groups, such as the Scandinavian, the Italian, the Irish, etc. Seasoning and cooking of foods may vary in these different races and special idiosyncrasies to certain types of food may be present. When one considers the individual food composition in the various racial diets, the differences may be more superficial than real. Slight variations in the preparation of the required food articles in many instances set the adjustment to supply the necessary chemical constituents.

**Obesity and Tuberculosis.**—A constant slight gain in weight, approximately one pound weekly, is very satisfactory, while the patient is undernourished, but once he has passed beyond his average normal weight, he should not be allowed to become unnecessarily fat. The stature of the individual is a determining factor. An excess of ten to twenty pounds beyond the normal weight point is usually sufficient. The accumulation of fat has never proved to be a factor in the healing of the tuberculous lesion and I have seen many patients show a satisfactory progress to recovery without carrying the additional burden of obesity.

**The Menu.**—(a) *Dietetic Principles.*—The principles of menu planning must take into consideration provision for an adequate supply of proteins, carbohydrates, fats, minerals and vitamins. Provision must also be made in the case of patients without gastrointestinal complications for roughage. The caloric intake must be adequate. The tuberculosis menu today postulates merely a moderately increased caloric intake and a moderate, relative and absolute increase in the protein constituents. This is necessary, owing to the fact that in tuberculosis there is a considerable breaking down of tissue which must be compensated.

(b) *Calories.*—We are, unfortunately, only too inclined to lay down mathematical formulæ on the subject of calories. We must remember that caloric indications vary greatly in the individual cases. A laborer may need 3000 to 3500 calories per day; a clerk may need only 2500 calories. It will be seen then that caloric indications vary greatly in health.

We must presume that they vary even more in disease when the metabolic processes are definitely upset. The healthy individual at complete rest needs

approximately 15 calories per day per pound. An individual weighing 150 pounds, at complete rest in bed, should have approximately 2250 calories. A healthy individual, who is not at rest will need a greater number. For instance, the adult in average activity will need 16 to 20 calories per pound per day. In tuberculosis, owing to the increased metabolism and tissue destruction, the number of calories should be increased. The number of calories, when indicated, may be increased by milk taken between meals. In planning a high caloric diet, one should also keep in mind such foods as butter, cream, meat, custards and ice cream.

We must not be content with a caloric estimate and disregard the appetizing qualities of the food. *We must consider the food in the calories as well as the calories in the food. In other words, we must give the patients their calories in the food they like, and if possible, in the food to which they are accustomed, provided this food contains the proper constituents in the balanced amount.*

(c) *Proteins.*—The proteins are especially essential in tuberculosis. They build new tissues, repair or renew exhausted tissues and, to a lesser degree, furnish body heat. The proteins are organic compounds containing nitrogen and are called the flesh formers. The proteins are such substances as myosin in meat, gluten in wheat, casein in milk and albumin in white of egg. Nitrogen forms the building element in the diet, the building blocks as it were. The fuel value of the proteins is of less importance.

It has been estimated that the proteins furnish about one-sixth of the body heat. The estimates vary, however. According to Voit, Playfair, and Gautier, 16 per cent. of the fuel value of food is derived from protein. Langworthy estimates the fuel value at 12 per cent. and Atwater at 15 per cent. Chittenden, on the contrary, makes quite a low estimate, 8.5 per cent.

(d) *The Protein Ration.*—Considerable difference of opinion has existed and still exists concerning the proper protein ration, both in health and in disease. Chittenden, for instance, contends that 60 grams a day is sufficient for the average healthy individual. Other investigators of merit claim that 100 grams a day are necessary.

It has been the tendency at all times and amongst all peoples to regard a high protein diet as the diet associated with both physical and mental activity. It has also been the tendency to attribute the success and progress of certain races to the fact that they are accustomed to a large protein ration in their daily food.

There is much for and against this hypothesis and the question can be considered as by no means settled. It seems quite probable that in relating high protein ration to prosperity the principle of cause and effect is being confused. The race or individual, for instance, who is prosperous is more apt to indulge in a richer diet, in larger amounts of meats and consequently in protein. A race, consequently, is not prosperous because it eats protein but eats protein because it is prosperous.

*The Source of Protein.*—As far as present indications go, for the average patient, the best source of protein lies in animal food. The foods rich in proteins are meats, brains, liver, lamb, beef, fowl; fish, such as mackerel, salmon, perch, cod, haddock, eggs, cheese and milk. The vegetable proteins are found in such

foods as lentils, whole wheat, peas. The vegetarian who is averse to the use of meat will find sufficient protein in these and similar vegetables. While sometimes the vegetable proteins are of low biological value, this is more than amply supplemented by the high biological value of the milk and egg proteins. For the average person, however, who is accustomed to a meat ration, we believe that the best source of protein is to be found, as stated, in animal food.

(e) *Carbohydrates*.—Carbohydrates are called "protein spacers" because by their use the amount of protein necessary is decreased. The carbohydrates are, if properly selected, easily assimilated, digestible and should form an important part of the dietary constituents. Carbohydrates, as the name implies, are composed of carbon, hydrogen and oxygen and are found as sugar in fruits and root vegetables and as starch in cereals. They are then, in reality, starch and sugar. They furnish strength and energy for both work and recreation and, in addition, supply heat to the body. It is estimated that the carbohydrates produce about one-half of the body heat.

The type of carbohydrates to be given is of importance. The best sources of carbohydrates for the tuberculous patient are such foods as cereals, like rice and oatmeal; potatoes, bread; fruits and vegetables. Excessive sugar is not desirable, particularly for patients who are inclined to be dyspeptic. Concentrated carbohydrates in the form of sugary desserts, candy, etc., are to be avoided because of the anorexia which may follow their use. If given, they are best taken after, not before or during the meal.

(f) *Fats*—Fats also take an important part in supplying heat, producing one-third of the bodily heat. The capacity of digesting and absorbing fat varies considerably with the individual patient. Fat, in the case of some patients, causes gastrointestinal disturbance and diarrhea. It is, in fact, rather characteristic that some individuals who develop tuberculosis seem to have had a dislike for fat prior to the onset of the disease. Many of these patients have never been able to take such foods as fat meats, bacon or ham.

As regards the source of fats, if we are limited to one food, we should say that the best source of fat, as far as the tuberculous patient is concerned, is butter. Large quantities of butter may be taken, thickly spread on bread, mixed with vegetables or in some similar fashion. Butter is palatable, digestive and up to five or six ounces a day may be taken with profit. Other valuable sources of fat for tuberculous patients are nicely marbled meat in which the fat is not too noticeable, such fish as salmon, shad, sardines, etc. Cream, cream cheese and milk are also valuable foods from the point of view of their fat constituents.

(g) *Minerals*—The importance of proper mineral balance both in health and in disease is not sufficiently appreciated. An adequate mineral supply is especially indicated in tuberculosis. Available evidence seems to show that the loss of mineral salts is higher in the tuberculous patient than in the normal individual.

The rôle of the minerals in the body is being more understood with our increasing studies of biochemistry, especially as it relates to minerals and vitamins. We now know that minerals such as calcium or phosphorus are essential to cell stabilization; that minerals such as iron are essential to the red cell; that minerals such as iodine are essential to other metabolic processes. We also know



from our experience that a diet deficient in mineral supply is ineffective and even disastrous. Calcium is present in milk, cheese, cream, eggs, cauliflower, dandelion and turnip greens and peas; to a lesser extent in cabbage, carrots and Brussels sprouts.

Phosphorus is found in such foods as lentils, dried peas, navy beans, white bread, and to a lesser degree in sweet and white potatoes, onions, spinach, cream, milk and American cheese. Sodium is found in such foods as rice, lentils and spinach. Chestnuts, baked potatoes and carrots are rich in potassium. Iron, one of the most important of the mineral constituents, is found in such food as liver, lean beef, oysters, spinach and other green leafy vegetables, yeast, white potatoes, navy beans and dried peas.

Such foods as cabbage, carrots and cauliflower contain sulphur.

While it is generally thought that a generous ration of fruits and fresh vegetables, particularly the green vegetables, will insure an adequate supply of minerals, *one must bear in mind that the mineral composition of various foods is subject to a wide variation dependent on the variations in the mineral content of the soil in which they are grown*. Additional minerals may have to be supplied to make up deficiencies which occur in this way.

(h) *Vitamins*—Vitamins are most important in proper balanced feeding for the maintenance of good health. *Vitamins may be defined as substances, the absence of which produce peculiar disease syndromes or a predilection to other pathologic manifestations in the living being.* At the present time, our knowledge is limited to a group of these substances which have been classified as vitamins A, B, C, D, E, G, and K. As these vitamin substances are isolated, their chemical structure is being determined so that their synthetic preparation becomes possible.

Vitamin A, when deficient, may produce such conditions as xerophthalmia, nutritional night blindness, keratomalacia, and a definite kind of follicular keratosis of the skin. It also is supposed to aid in maintaining resistance of the mucous membranes against infection, to stimulate epithelial growth, and is of questionable value in urinary lithiasis. More recently it has been shown to be of some value in anemias and agranulocytosis.

It is found in chlorophyll-containing foods, such as peas, peppers, asparagus, the outer leaves of lettuce, yellow vegetables and fruits, such as carrots, apricots, peaches, bananas, yellow tomatoes and food of animal origin, such as eggs, whole milk, liver, and fish liver oils.

Vitamin B complex has been fractionated into six different factors. These are B<sub>1</sub>, or thiamin, which has been isolated chemically and is prepared synthetically at this time, and the usage of which is mounting to enormous volume. It is the anti-neuritic factor and also prevents beri-beri. It is heat labile.

B<sub>2</sub>, also known as vitamin G, or as riboflavin, the pellagra-preventative factor, is also supposed to be identical with or similar to nicotinic acid. It is heat stable and is very important as a nutritional factor.

B<sub>3</sub> is a growth-promoting factor.

B<sub>4</sub> seems to have special value in experimental work in preventing specific types of paralysis in rats and chicks.

B<sub>5</sub> and B<sub>6</sub> are still questionable as to their exact importance as parts of the B complex, while B<sub>1</sub> and B<sub>2</sub> have been isolated and can be prepared synthetically.

The foods which contain the B complex in larger amounts may be listed as dry yeast, wheat germ, wheat flour, liver, cottonseed flour, lean beef, egg yolk, and spinach.

Vitamin B, when deficient, has been noted to be a cause of nausea, loss of appetite, loss of weight, lack of vigor, general weakness, digestive disturbances, colitis, constipation, and finally, symptoms more referable to the nervous system.

Vitamin C, which is both preventative and curative for scurvy, also is called ascorbic acid or cevitic acid. More recently it has been stated that some relationship exists in its deficiency to the condition of hyperthyroidism, diabetes, and Addison's disease. It apparently also is necessary in combating infections in the body. It is found more liberally in such foods as oranges, lemons, limes, ripe tomatoes, horseradish, broccoli, brussels sprouts, cauliflower, asparagus, green beans, black currants, strawberries, gooseberries, dandelion greens, grapefruit, parsley, both red and green peppers, and pineapple. Many other vegetables contain this vitamin in lesser quantities.

It is necessary to state here that many foods contain more than one vitamin. Cabbage, for instance, contains vitamins A, B, and C in good quantities. The same is true of carrots and some other foodstuffs.

We are inclined to associate diet deficiency in vitamin D with the condition known as rickets. There is, in addition, a very definite but little understood relationship between vitamin D and sunlight. It is found, for instance, that the child suffering from rickets will improve very materially as soon as the diet is changed to include substances rich in vitamin D. The same child, however, will show similar improvement even without change of diet if exposed to sunlight, either artificial or natural, in the required degree. Furthermore, without change of diet and without exposing the child directly to sunlight, if the food lacking in vitamin D is exposed to the ultraviolet ray, it is noted that similar improvement occurs as under the two previous conditions.

Vitamin D is produced by the action of ultraviolet rays upon cholesterol found in the secretion of the sebaceous glands of the skin. It is also produced by the irradiation of ergosterol with ultraviolet rays (viosterol).

Recent research dictates that this vitamin is most important in aiding the deposition of mineral salts, particularly calcium, into the tissues. This results in an increase in the absorption of calcium from the intestinal tract when it is fed. Further discussion concerning this is given under the section on chemo-therapy as it relates to the use of calcium in tuberculosis.

Vitamin D is found in large quantities in cod-liver oil, egg yolks, milk and butter.

Vitamin E is known as the anti-sterility vitamin and is supposed to influence the processes of reproduction. This vitamin can be stored in the human body over a long period of time, is widely distributed and therefore easily obtainable. Experimental animals consuming a diet vitamin E free, over a long period of time, develop atrophy in the male of the germinal epithelium of tubules in the testes, and in the female the ability to properly imbed the ovum, which results in resorption or abortion.

Vitamin K has to do with the clotting of blood. This supposedly is tied up with bile salts, but the exact mechanism, at this time, has not been definitely shown.

This résumé of vitamin substances is given because of their importance in regulating cell stability and engendering cell and tissue resistance to improve general health. Symptoms may occur, indicating deficiencies and direct the need for supplemental feedings.

**Sample Menu.**—The following menu has been used by me for a number of years, and based on additional knowledge in nutrition that has been developed, I have modified it. I term it the "mixed vitamin diet." It contains all of the food substances, protein, fat, carbohydrates, minerals and vitamins in ordinary balanced amounts.

This diet is well tolerated by the average tuberculosis patient and modifications, because of idiosyncrasies, very rarely have to be made. Under certain symptomatic indications, additional vitamin concentrates and minerals are added. For instance, in the presence of loss of appetite, intense fatigue or nervous debility, vitamin B, in the form of Brewer's yeast, is frequently added. The mineral salts are also frequently given in the form of a special mixture derived principally from the natural source of a bone meal, plus alfalfa ash, with traces of an organic iodine.

#### THE MENU.

Soup Cream of puree.

Fish: Fresh cod, halibut, bass, boiled with cream sauce or broiled. Fresh lake fish, boiled or broiled.

Meats Chicken, turkey, or lamb occasionally. Small piece of rare lean beef two or three times a week. *Calves' liver* two or three times a week.

Vegetables: All vegetables in abundance, especially carrots, lettuce, cabbage, string beans, tomatoes and spinach.

Cheese Any mild variety—cream cheese preferred.

Desserts. Cream and egg desserts of all sorts, namely blanc mange, Bavarian cream, floating island, cup custard, junket, soft rice or bread pudding. Gelatin desserts made with fresh fruit juice flavoring. Very little sugar in all desserts. Stewed soft fruits may be taken in good amounts, cooked with little sugar, and are best taken with or after a meal—never before. Cream may usually be freely taken. Very little sugar.

Fruits Oranges, orange juice, lemon juice, grapefruit, raspberries, applesauce and pineapple.

Bread Whole wheat, made with milk.

Butter: Fresh butter or salt butter freshened by working it over in fresh water. *Six pats of butter daily. Two teaspoons of cod-liver oil three times daily.* The butter should be increased if the patient takes cod-liver oil concentrates.

Drinks: Cream, cocoa, milk and water. *Four glasses of milk daily.* ½ glass tomato juice daily.

Cereals Fine-grained varieties, well cooked, such as farina, wheatena, oatmeal, cream of wheat, etc.

Eggs: In all forms, except fried. *The yolks of two eggs each day in orange juice or in milk.*

**Special Diets.**—It occasionally becomes necessary, because of complications which arise in the course of treatment, to order a special diet to adjust the diet formula to meet the needed and usually temporary indication. The diet formulæ on the following pages may be useful.

GASTROINTESTINAL DIETS (*Continued*).*Allowed:**Not Allowed:*

Cereals: ( <i>continued</i> )	Wheatena, farina, which two need not be strained. Farinaceous foods as macaroni, spaghetti, noodles and rice	
Breadstuffs:	White bread only, toasted or stale	Whole wheat bread, rye bread, all quick breads, fresh yeast bread, cakes
Condiments:	Salt	All spices, condiments (except salt), vinegar, mustard, paprika, catsups and sauces
Jam & Jelly:	None	
Beverages:	Water, milk, cocoa, weak tea, cream	Coffee, strong tea, chocolate, rich malted drinks
Nuts:	None	
Desserts:	Plain gelatins and jellies, custards, junkets, tapioca, rice or cornstarch puddings, farinaceous puddings, milk custards and pudding. Strained fruits	Rich pastries, cake, sweets, ice cream, hot puddings, puddings containing raisins or dates

Gastrointestinal diet No. 2 differs from No. 1 in that certain meats are allowed, namely: Scraped beef, finely minced white meat of chicken and fish, minced or ground lamb, crisp bacon.

Those not allowed: Beef prepared any way except scraped, mutton, fat fish, dark meat of chicken, dark meat of fish, pork, veal; prepared, dried or smoked meats. No fried meats are allowed.

The vegetables may be eaten unstrained if they are well cooked and not of the class too rich in cellulose.

The diets also differ in the number of feedings; No. 1 being comprised of six small feedings; No. 2 having only the three feedings.

## DIARRHEA DIET.

*Allowed:**Not Allowed:*

Meats:	Lamb, chicken, scraped beef, white meat of chicken, oysters, crisp bacon	Pork, veal, beef, mutton, fish high in fat, fried meats, corned beef, chopped beef, liver, twice cooked meats
Eggs	Soft boiled or poached eggs	Hard cooked; fried
Cheese	Cottage cheese, mild cheese	Highly ripened cheese
Potatoes	Mashed, rice, baked or boiled Irish potato	Fried or buttered potato, sweet potato
Vegetables:		All
Fruits:		All
Cereals:	Rice, farina, puffed rice, cream of barley, farinaceous foods as spaghetti, macaroni, noodles, tapioca	Rolls, oats, corn meal mush, all wheat cereals containing bran, corn, except sieved and made into soup
Desserts:	Cereal and farinaceous puddings, simple cake, custards, plain jello	Pastry, sweets, rich cakes, spiced cakes
Breadstuffs:	Day old bread, dry toast, plain rolls, toasted crackers	Fresh yeast breads, quick breads, fancy rolls and bread, whole wheat bread and rye bread



## LOW FAT DIET

	<i>Allowed:</i>	<i>Not Allowed:</i>
Meats:	Lean beef, lamb, chicken, veal, dried beef. Sea food with low fat content.	Any meat high in fat content as pork, bacon, fat fish
Eggs:	Occasionally	
Cheese:	Cottage cheese—no cream	Cheese high in fat content
Potatoes:	Without butter	Fried, or seasoned with butter
Vegetables:	All	
Fruits:	All	
Cereals:	All	
Farinaceous Foods:	All	
Desserts:	Simple puddings, custards, jello, ice	Cakes or any desserts high in fat
Breadstuffs:	All	
Condiments:		All
Jam & Jelly:	Jelly	Jam
Nuts:		All
Beverages:	Tea, coffee, skimmed milk, cocoa made of skimmed milk, postum, etc	Whole milk, cream
Soups:	Fat-free broth, soups, cream soups made with skimmed milk	Soups high in fat content

The low fat diet is indicated in gall-bladder conditions. This diet, because of a low caloric value and low content of vitamin A and D, is an inadequate diet. Haliver oil D-250 or carrots and Viosterol are given, or the fat content is raised as soon as the condition of the patient permits, by adding butter, cream and more eggs to the diet to supply such vitamin deficiency. Fats of high melting point, and which have no value for vitamin content, such as meats high in fat, are not added until the patient is in condition to tolerate a normal diet. The caloric value of this diet is about 1600 with about 90 grams of protein

## GASTROINTESTINAL DIETS.

	<i>Allowed:</i>	<i>Not Allowed:</i>
Meats:	None	
Eggs:	Soft-cooked, poached, coddled	Fried, hard cooked, baked, scrambled.
Cheese:	None	
Potatoes:	Mashed, baked, riced, double baked	Fried, plain boiled, creamed, es- calloped
Vegetables:	Cooked, strained and purced only, peas, carrots, spinach, string beans, beets, squash, lima beans, turnips,* rutabagas,* cauliflower, asparagus	Any raw vegetables, any vege- table having a great deal of cellulose, as cabbage, celery, let- tuce, radishes; acid vegetables as tomatoes, strong flavored vege- tables as onions
Fruits:	Stewed or canned, applesauce, peaches, pears, sieved prunes, plums, apricots, cherries and canned fruit juices.	Any raw fruit, canned pineapple, rhubarb, raw fruit juices
Cereals:	All thoroughly cooked and strained; oat- meal, Wheatena, cream of barley, hominy grits, cornmeal, cream of wheat and	All dry, prepared cereals

\*These vegetables cause gas to form in some cases.

DIARRHEA DIET (*Continued*).*Allowed:**Not Allowed:*

Condiments:	All
Jam & Jelly:	All
Nuts:	All
Beverages:	Boiled milk, cocoa, postum
Soups:	Broth, cream soups
	Vegetable soups

Tuberculous patients are prone to attacks of diarrhea. During such attacks no food is given that tends to aggravate the condition. All foods high in fat and high in cellulose are forbidden. These include fat meats, fruits, green vegetables and cereals or breadstuffs containing bran.

## BLAND DIET.

*Allowed:**Not Allowed:*

Meats:	White meat of fish and chicken, crisp bacon, sweetbreads, oysters	Pork, veal, beef, lamb, mutton, fat fish, dark meat of chicken, corned beef, fried meats, liver.
Eggs:	Soft cooked, poached, coddled, baked, hard cooked	Fried
Cheese:	Cream, American, cottage cheese	Highly ripened cheese
Potatoes:	Mashed, riced, baked, double baked, boiled, creamed, sweet potato	Fried
Vegetables:	Sieved peas, spinach, beets, parsnips, squash, carrots, asparagus, string beans	Tomatoes, cabbage, cauliflower, onions, sauerkraut, turnips, rutabagas, celery and all raw vegetables
Fruits:	Cooked peaches, pears, apples, bananas, strained orange juice in small amounts	Pineapple, cherries, prunes, berries, all raw fruits, acid fruits
Cereals:	Farina, strained oatmeal, rice, puffed rice. Farinaceous foods as macaroni, spaghetti, tapioca, noodles, sieved corn	Cereals including bran, as Wheatena, post wheat meal, puffed wheat
Breadstuffs:	Day-old white bread, sponge cake, plain butter cake and cookies	Breads of flour containing bran, pastries, quick breads, spice cakes
Condiments:	Salt	
Jam & Jelly:		Jam
Beverages:	Cocoa, milk and cream	Tea, coffee

The patient on a diarrhea diet on improvement may have his diet changed to one that is bland. This is more liberal than the diarrhea diet in that sieved bland vegetables and fruits are added. Meat high in fat, vegetables which are gas formers and are high in cellulose, acid fruits and foods containing bran are still prohibited. Though uninteresting, this is an adequate diet.

## NON-RESIDUE DIET.

*Allowed:**Not Allowed:*

Meats:	Beef, lamb, fowl, boiled, broiled or roasted; crisp bacon, all sea foods, calves' liver	Pork, veal, fried meats, twice cooked meats, corned beef, chipped beef, liver, except calves' liver
Eggs:	Soft-cooked, poached, scrambled, coddled, hard-cooked	Fried
Cheese:	Any cheese	

NON-RESIDUE DIET (*Continued*).

	<i>Allowed:</i>	<i>Not Allowed:</i>
Potatoes:	Mashed, riced, creamed, buttered, baked, sweet potato	Fried
Vegetables:	Sieved peas, strained tomato, sieved spinach, beets, parsnips, squash, string beans, asparagus	Gas-forming vegetables, as cabbage, cauliflower, onion, sauerkraut. Vegetables of coarse fibre, as some string beans, old beets, rutabaga, spinach, kale stems, celery, raw vegetables
Fruit:	Canned fruits, strained orange juice and grapefruit juice, fruit juices	Canned pineapple, raw fruits, prunes, berries
Cereals:	Farina, strained rolled oats, puffed rice, cornflakes, rice, farinaceous foods as spaghetti, tapioca, noodles, macaroni, sieved corn	Cereals including bran, as Wheatena, puffed wheat, etc.
Breadstuffs:	Day-old bread Plain cakes and cookies	Breads of flour containing bran; pastry
Condiments:		All, except salt
Jam & Jelly:	Jelly	Jam
Beverages:	Coffee, cocoa, tea, milk, cream	

## CHAPTER XVII.

# SALT-RESTRICTED DIETARIES IN TUBERCULOSIS.

EDGAR MAYER

### HISTORICAL.

The nutrition of tuberculous patients underwent no outstanding change until about 10 years ago when Max Gerson proposed feeding such patients a salt-restricted dietary. Believing that various diseases arise or flourish on the basis of abnormal mineral relations in the body he sought to influence these diseases, including tuberculosis, by direct modification of the mineral balance. Salt-restriction, with a view to dehydration, had been previously introduced by Strauss in 1903 for the treatment of kidney conditions. Thereafter this therapy found application also in cardiac, circulatory, cutaneous and other disorders. Its further extension to the tuberculosis field, in combination with specially selected and specially prepared foods, is, however, primarily due to Gerson, whose pioneer labors in this field merit the fullest recognition. The application of salt-restriction, of course, merely *modifies* the nutritional factor in the accepted treatment of tuberculosis without affecting the validity of the other two leading factors.

Gerson was led to his salt-restricted tuberculosis treatment partly by systematic research and partly by accidental circumstances. For many years he had studied the rôle of the *mineral metabolism in relation to migraine*. In this disease salt-restriction combined with particular diets had given him good results. Some of his migraine patients happened also to have tuberculous lesions which healed concurrently with the migraine. These results attracted the attention of Ferdinand Sauerbruch about 1925, who thereafter subjected Gerson's dietary proposals to extensive clinical study in the different forms of tuberculosis in the Munich and Berlin University surgical clinics. These researches were committed by Sauerbruch to A. Herrmannsdorfer, who on Sauerbruch's initiative had been for some time engaged in an investigation of the influence of acid diet on the healing of wounds. The clinical study of the Gerson diet was supplemented by a large amount of intensive research work as a result of which Herrmannsdorfer modified this diet in some respects though Gerson's salt-restriction was retained unaltered. This modified dietary is now known as the Herrmannsdorfer-Sauerbruch diet. Gerson has also several times modified his original directions, which must be taken into consideration when discussing or employing the Gerson diet. The undermentioned outline of it represents its latest form. The perception of the far-reaching import of Gerson's dietary proposals must be credited to Sauerbruch.

### CHARACTERISTICS.

Before entering into the theoretical foundations of the salt-restricted dietary treatment of tuberculosis and of the observed clinical results, the general characteristics of the Gerson and Herrmannsdorfer-Sauerbruch methods may be

briefly considered. Important differences between the two diets and lists of the foods which are prohibited and permitted in each, as well as specimen menus, are appended in the tables. Neither diet permits table salt in cooking or on the table. With rare exceptions no foods containing table salt are permitted, so that these diets contain merely the sodium chloride which is naturally present in the different foods. When the diets are prepared as directed, their salt (sodium chloride) content appears to average about 3 to 4 grams according to the nature and source of the component foods and the amount of food which is ingested. The selection and preparation of the foods for the table is conducted in a manner calculated to ensure a high and varied vitamin, ferment and mineral content. Both diets are rich in fat but low in carbohydrate, the carbohydrate content of the Gerson diet being somewhat higher than that of the Herrmannsdorfer modification. Protein is low in the former, moderately high in the latter. Gerson permits only 100 grams of meat per week, Herrmannsdorfer about 500 grams.

In the Herrmannsdorfer-Sauerbruch diet the protein, fat and carbohydrate ratio is now definitely fixed at 1.5:2.7:4 and this distinctive feature is considered very important by Herrmannsdorfer.

The Herrmannsdorfer-Sauerbruch diet covers the fluid requirement chiefly by means of milk but in the Gerson diet it is covered almost entirely by raw vegetable juices and raw fruit juices. While both diets employ uncooked foods along with cooked ones the Gerson diet has a larger proportion of the former, in addition to which it makes systematic occasional use of so-called raw food days on which only uncooked foods are allowed. The Gerson diet is alkaline-ash while an acid-ash character is claimed for the Herrmannsdorfer-Sauerbruch diet. The two methods show more or less subordinate differences, besides the foregoing leading ones, which relate to prohibited and permitted foods and the preparation of some of the latter.

From the foregoing considerations we may characterize the Gerson and Herrmannsdorfer-Sauerbruch diets as follows: The Gerson diet is predominantly vegetarian, alkaline-ash, protein-poor, fat-rich, carbohydrate-poor, with table salt practically totally excluded. The Herrmannsdorfer-Sauerbruch diet is a mixed diet, acid-ash, moderately protein-rich, fat-rich, decidedly carbohydrate-poor, with table salt practically totally excluded.

Both Gerson and Herrmannsdorfer give a mineral mixture with a high percentage of calcium lactate and calcium phosphate and phosphorized cod-liver oil by mouth. In addition to these medicaments Gerson sometimes employs particular hormones and irradiated cod-liver oil.

Whereas Sauerbruch and Herrmannsdorfer limit their diet almost exclusively to the tuberculous field Gerson employs his treatment not merely in tuberculous but also in a variety of internal and cutaneous disorders.

### THEORETICAL FOUNDATIONS.

Gerson's original diet was almost entirely vegetarian, carbohydrate rich and salt-restricted, and was intended to alkalinize. Herrmannsdorfer modified it because he believed it desirable to take it into account the then available experimental

and clinical evidence in the literature regarding the influence of the different dietary components on the tuberculous disease process. Thus, animal experiments appeared to show that a considerable protein intake diminishes the susceptibility to infections and that a generous allowance of fat and lipoids augments the body's defensive powers. A high carbohydrate content on the contrary was believed to favor extension of tuberculosis. The susceptibility to infection was also thought to be related to a high water content of the tissues so that dehydration would favor resistance. Further, the vitamins were thought to raise the defensive forces. In addition, Herrmannsdorfer's results with acid diet in the dietary treatment of wounds, wherein he attempted to reduce the blood buffers by a concentration of acid in the wound, led him to regard an acid-ash diet desirable also in the dietary treatment of tuberculosis, though, owing to the chronic nature of this disease, he aimed at a much feebler acid reaction than in his wound-healing diet.

The diet formulated by Herrmannsdorfer on these foundations contains in about 2800 calories, approximately 90 grams protein, 160 grams fat (not including 40 grams cod-liver oil) and 240 grams carbohydrate. The caloric intake for pulmonary patients is from 45 to 50 calories per kilogram of body weight.

Gerson's own modifications of his original diet relate chiefly to the protein content, which now averages only about 45 grams, and to supplying the fluid requirement almost entirely with juices extracted from raw vegetables and raw fruit instead of milk and other beverages. Gerson also reduced the carbohydrate content of his diet. Besides these modifications he makes increasing use of interspersed days on which only raw food is allowed.

The main objectives of both diets are to dehydrate the tissues and to modify the body's mineral balance. On the basis of findings by various authors which seemed to show that a relatively dry diet favors the curative process in tuberculosis, Herrmannsdorfer now allows practically no water for drinking but covers the fluid requirement mainly with milk. The high proportion of uncooked vegetables and of fruit, as well as fruit juices, furnishes much moisture and the lack of water does not appear to inconvenience patients after the first few days.

The preparation of the foods does not differ greatly in the two diets. Both demand that vegetables shall not be pared or scraped but cleaned by brushing and that they shall be steamed and not cooked, the steaming being performed in covered containers without water but with sweet dairy butter. Meats, except pork, are done slightly rare, broiling being preferred. The cooked foods are directed to be freshly prepared and eaten when ready. Warming over of dishes and the use of self-cookers are to be avoided. All these and other methods of preparation seek to preserve the vitamin, ferment and mineral content of the foods. The selection of the permitted foods and the form in which they are given also seek to assure the presence of adequate amounts of these constituents and in the case of the Herrmannsdorfer modification to yield an acid-ash diet. Both Gerson and Herrmannsdorfer make use of several preparations for masking the lack of table salt, such as certain meat extracts, nutrient yeast and others, some of which are not made in this country.

## CLINICAL RESULTS.

In 1926 Sauerbruch and Herrmannsdorfer<sup>1, 2</sup> published preliminary observations of the effects of the Gerson diet and in 1928 they reported results in about 180 cases treated with their modification, since when Herrmannsdorfer<sup>3</sup> has reported further results. The authors claimed for the treatment, without accessory therapies, curative effects not only in skin, bone, joint, lymph node and mucosal tuberculosis, but also in the pulmonary form. In skin tuberculosis they observed striking changes, such as successive disappearance of inflammation, encrustation of ulcers, desquamation, formation of connective tissue and development of pale smooth cicatrices; in lupus vulgaris regression of perifocal inflammation and disappearance of nodules. In lymph node, mucosal and urogenital tuberculosis sinuses dried out, ulcers shrank, suppuration ceased, cicatrization set in. In some severe perforative bone and joint lesions remarkable improvements were noted. Bone tuberculosis showed desiccation and cicatrization and closure of small and medium-sized sinuses. Pulmonary patients showed accelerated fibrosis, cicatrization and shrinkage; in some sputum diminished and frequently became negative. Striking weight gains from 1 to 70 pounds were noted. Bilateral cases with one incavitated side improved so much under the treatment that operative interference on the less affected side was rendered possible.

In 1929 Gerson<sup>4, 5, 6</sup> published a retrospect of the results with his diet up to that time and in 1930 and 1931 he reported results under further modifications of the same. For the modified diet he claims very favorable and more rapid results in pulmonary tuberculosis, with obliteration or healing of cavities in severe cases and an inhibitory influence on hemorrhage. Reported cases of healed cavities were controlled roentgenologically by Hohlfelder.

Sauerbruch and Herrmannsdorfer's publication of their results with the Herrmannsdorfer modification led to subsequent study of this method by numerous German and some other investigators, with conclusions that diverged in many instances from those recorded by the proponents of the method. Thus while Jesionek<sup>7</sup> and Bommer<sup>8</sup> reported striking curative effects in lupus, and while Schueller,<sup>9</sup> Rehn, Nather, Burkhardt, Glaser and others noted favorable results in bone and other tuberculous forms, a number of other authors failed to confirm a noteworthy influence on the pulmonary process. Among these were Baumeister, Andersen, Apitz, Blumenfeld, Mueller, Bettmann and Liesenfeld.

In 1930 Sauerbruch and Herrmannsdorfer<sup>10</sup> published a reply to critics wherein they expressed their belief that the unfavorable opinions were mostly founded on inadequate clinical trials or on faulty and not always unprejudiced application of their method.

In this country the Gerson and Herrmannsdorfer-Sauerbruch diets have so far found but little application. By courtesy of Sauerbruch, Herrmannsdorfer and Gerson I was able to study these dietaries at first hand in Germany in 1928 and subsequently treated a selected group of pulmonary cases at Saranac Lake, N. Y., on the original Gerson diet, reserving the Herrmannsdorfer modification for future study. The results in this series were reported by me<sup>11</sup> in 1929.

Twenty far-advanced pulmonary patients, aged between 22 and 33, who had failed to respond to two or three years of routine treatment were maintained on the Gerson diet for six months. Substantial weight gains, diminution of sputum but without loss of tubercle bacilli, definite clearing in the lungs as shown by physical and roentgenologic examination, loss of symptoms in intestinal complication, diminution of fatigue, of pains in chest and of alimentary disturbances were noted in the course of the treatment in various cases but it was impossible to ascribe improvement to the diet alone.

Emerson<sup>12</sup> in 1930 and Banyai<sup>13</sup> in 1931 reported encouraging results with modified forms of these diets in pulmonary cases. The Herrmannsdorfer-Sauerbruch modification has recently been studied in several American tuberculosis hospitals, reports on which are not yet available.

*Cutaneous Tuberculosis.*—A number of years have elapsed since Gerson, Sauerbruch and Herrmannsdorfer first published their results. In the interval much additional research work has been done in Germany and a very important contribution to our knowledge of the effects of salt-restricted therapy was made by Doerffel<sup>14</sup> in 1932. This investigator has presented most convincing results with macroscopic, microscopic and cultural studies on 51 patients with cutaneous tuberculosis treated with the Herrmannsdorfer-Sauerbruch dietary. In the great majority of these cases the results were excellent. After 12 to 14 days of the diet an inflammatory reaction of the cutaneous lesion, with an areola comparable to that seen following injection of tuberculin, takes place. Then gradually the lesion becomes dry and the inflammatory infiltration begins to resolve. Finally the apple-jelly nodules disappear and in the course of months only small depressed scars remain. In favorable cases the entire lupus lesion heals with surprisingly good cosmetic results, the scars being smooth and delicate.

Histologic studies revealed changes characteristic of healing. After approximately 14 days of the diet all edema had disappeared and one was able to see clearly the quantitative and qualitative changes which the lupus infiltrates had undergone. The vessels, especially the elements of the vascular walls, and the young, richly vascularized connective tissue spread out into the infiltrated area which surrounded it and which divided it into small nets. In this way the infiltration disappeared, particularly when the fibroblasts developed, these coming in great part from the elements of the vascular walls.

Bacteriologic studies revealed that tubercle bacilli were apparently decreased in virulence and in 14 cases in which cultures were made several times they disappeared in every instance. Approximately half of the cases had shown positive cultures before the diet was begun. It is suggested that this decreased virulence is due possibly to stimulation of the activity of the reticulo-endothelial system by the diet.

Studies of the *blood picture* also showed a favorable influence on the entire organism which corresponded with the visible improvement and with the favorable histologic changes. The skin under this diet also reacted more severely than usual to old tuberculin, ultraviolet light, chrysarobin, croton oil and mustard plaster.



4. Sedimentation of erythrocytes is at first increased in nearly all cases and then diminishes, which indicates that the diet effects a modification in the body.

5. The most important practical conclusion is that although one cannot expect severe pulmonary processes, particularly large cavities embedded in indurations, to heal under the diet alone, the diet should nevertheless be employed for patients who fail to improve under the customary sanatorium nutrition. In many such cases, excepting severe exudative processes and intestinal tuberculosis, the diet can bring about a change in the general condition which induces definite healing or renders the patients suitable subjects for other therapeutic measures, particularly operative ones.

The special, strongly acid diet which Herrmannsdorfer employed in his wound-healing experiments is recommended by him also for severe suppurative (mixed infection) tuberculous affections. He states that transient application of this markedly acid nutrition may also give renewed impetus to healing in other tuberculous forms. This diet is not given longer than three to four weeks and its acidifying action is reinforced by simultaneous oral administration of one or other of several acidulating agents such as phosphoric acid, calcium chloride or hydrochloric acid. Details of this special "Acid" Diet are given in "*Kochbuch fuer Tuberkulose*," by A. and M. Herrmannsdorfer.<sup>16</sup>

### PRACTICAL APPLICATION.

The salt-restricted dietaries of Gerson and Herrmannsdorfer-Sauerbruch, particularly the latter, offer a remarkably wide variety of foods. Difficulties attending their use therefore are due largely to their salt poverty. Their necessarily lengthy application makes it imperative to assure adequate palatability of the food. Many years ago Strauss<sup>17</sup> gave directions for rendering unsalted food palatable. Gerson<sup>18</sup> has furnished similar directions and M. Herrmannsdorfer<sup>19</sup> has elaborated these recently. The absolute necessity for securing palatability has been repeatedly stressed by Herrmannsdorfer who states that in the salt-restricted dietary treatment of tuberculosis the kitchen technic is of decisive importance. It must be laid down as an axiom that unless the kitchen is prepared to devote constant strict attention to the adequate and skillful seasoning of the different foods as well as their proper presentation, it will be impossible to carry through the treatment successfully for any length of time.

The practical application of the salt-restricted tuberculosis dietaries in institutions makes great demands on physicians, dietitians, kitchen and personnel. The absolute need for untiring harmonious coöperation by all concerned cannot be overemphasized. Without this prerequisite the treatment cannot be applied satisfactorily.

*Preparation.*—Directions for preparing the Gerson Diet have been given by Gerson<sup>20, 21, 22</sup> in his book entitled "*Meine Diaet*," published by Ullstein, Berlin, but the most recent directions are those he has given in the *Zeitschrift fuer Aerztliche Fortbildung*, 1930, 11 and *Muenchener Medizinische Wochenschrift*, 1930, 23. Herrmannsdorfer<sup>23</sup> has given exhaustive directions with over 300 quantitative menus and tables for the Herrmannsdorfer-Sauerbruch diet,

which also contains useful notes for physicians, in his "*Kochbuch fuer Tuberkulose*."<sup>16</sup>

Before the treatment is instituted the necessary equipment should be secured and the arrangements for preparing and serving the diet given careful thought. The diet foods should be stored and prepared separately from other foods. Constant vigilance is needed to prevent possible contamination of the diet foods or of patient's utensils with common salt. The cooked foods must reach the patient quite hot, as cool unsalted food causes aversion and jeopardizes the entire therapy. The foods must be presented in an appetizing form which should be varied frequently. Meals must be served very punctually. It is of the utmost importance to assemble and inspect the returning trays after every meal so that each patient's cooperation may be determined all the time and corrected if necessary. In view of the great importance of the quality of the foods which are used for the diets the selection of the raw materials should receive strict attention in accordance with the directions. The weighing and preparation of the foods and the traying and serving of the meals must be constantly supervised by a highly conscientious individual specially detailed for this purpose.

The physician in charge of dieting patients must exercise untiring supervision over every phase and aspect of the whole treatment. He must keep in constant touch with the dietitian. He will keep an eye on the quality of the raw materials, the prescribed preparation of the foods in the kitchen and the returning trays besides controlling medication, laboratory and x-ray work, etc. The dietary patients must be entirely segregated from other patients. Possible smuggling of table salt must be guarded against. Medicines must be taken in the presence of the nurse. The caloric intake must be regulated in accordance with the patient's weight. In the case of the Herrmannsdorfer-Sauerbruch diet, total calories will be increased with increasing weight of undernourished patients and reduced when normal weight is attained, and the relative proportions of protein, fat and carbohydrate as laid down by Herrmannsdorfer will be maintained regardless of the total calories. Of great importance naturally is the proper selection of the cases both from the standpoint of the diagnosis as well as from that of likely cooperation by the patient. Herrmannsdorfer is of the opinion that the use of the diet is always justified when the impairment of the patient's general condition by the disease prevents strong resistance to the same, and particularly also when patients have failed to respond to other therapies. In this connection Bausingaertner's<sup>24</sup> recent study of the Gerson and Herrmannsdorfer-Sauerbruch diets in pulmonary cases is of interest. He concludes that the diets exert no notable influence on predominantly suppurative inflammations, i. e., those rich in leukocytes, but that in inflammations with predominantly exudative character the exudation-inhibiting action of the diets becomes evident. He considers it deplorable that the advantages which result from this dietary treatment when employed in the right cases should remain unused.

Gerson and Herrmannsdorfer differ as regards the general conduct of the treatment. Gerson declines the use of accessory therapies, such as pneumothorax, phrenico-exsufflation and sun lamp, whereas Herrmannsdorfer favors these and other aids. Gerson employs no soporifics and even dispenses with rest in

reclining chairs for ambulatory patients, employing bed rest where there is fever and in severe cases. He maintains that the dechlorinated organism is more sensitive toward the customary dosages of medicaments and light than the organism under an ordinary diet. X-ray treatment is widely thought to be incompatible with the dietary treatment.

The physician's foremost aim must be to secure from the start and to maintain at all costs that harmonious attitude within the institution toward the dietary therapy which as I have stated is a prerequisite for satisfactory results. In hardly any other therapy is the physician's personal supervision and authority so essential as in this therapy. Without these the discipline of a group of patients cannot long be maintained. Without these also the continuous efficient coöperation of all concerned is unattainable.

Having regard to the many requirements, the treatment, when properly applied, will yield the best results in institutionalized patients while its application elsewhere will frequently fail.

Under this nutritional therapy the majority of a group of properly controlled patients shows remarkable morale and enthusiastic coöperation. A very striking phenomenon is the extremely small wastage of food. When properly handled the patients clear their plates almost entirely at each meal but the longer the treatment is maintained the more necessary becomes variety in the menus and varied seasoning of the foods. As a rule it is quite possible to keep many patients on the diets for a year or longer. Schematization of the menus must be strictly avoided and concessions made where necessary. When patients are taken off the diets and return to the customary nutrition they appear in many cases to maintain their added weight well or even to increase in weight slightly for some weeks thereafter. That would seem to conflict with the view expressed by some authors that the striking weight gains are in reality due to water retention in the body.

In very severe pulmonary and other cases and particularly in *intestinal tuberculosis* the diets may have to be modified at the start and gradually brought up to the specified requirements.

In considering the cost of the dietary treatment it is necessary to bear in mind the small wastage of food, the small amount of meat that is permitted, the relatively little medication, and the surprisingly rapid physical improvement. On the other hand the high quality of the materials and the additional supervision and help which the treatment entails cannot be ignored. In general it may, however, be stated that under proper management the cost of this therapy is by no means prohibitive.

#### A NEW MODIFICATION.

Many efforts have been made to facilitate the use of salt-restricted diets by means of so-called salt substitutes, all of which have proved disappointing. They are composed of substances having a more or less salty taste but contain no sodium chloride. To mask the lack of table salt, flavoring agents of many kinds, such as yeast preparations and salt-free meat extracts, have been recommended, as well as special culinary methods which develop aromatic principles that

compensate to some extent for table salt withdrawal. All these procedures are very troublesome.

Failure to compensate efficiently and easily for the withdrawal of table salt led Keining and Hopf<sup>25</sup> to reinvestigate the action of common salt in the body and to attempt the removal from it of its undesirable effects. Their results are of great interest and may find extremely important practical applications.

*Salt.*—Keining and Hopf point out that common salt is derived from brine springs or other natural sources in which sodium chloride is always accompanied by potassium, calcium and magnesium combinations. In the course of the manufacture of table salt from natural salt sources the associated potassium, calcium and magnesium salts are almost entirely removed, leaving practically pure sodium chloride. Prolonged consumption of this sodium salt is believed by Keining and Hopf to derange the normal cation relation in some people, which gradually enriches the body's sodium but impoverishes its potassium, calcium and magnesium content. Such derangement of the cation environment alters the colloid structure of the cells, affects their response to stimuli, disturbs conduction of stimuli and lays the foundation for sympathetic disturbances which in turn favor the apparition of various disorders such as skin stigmata, allergic diseases, etc. While table salt withdrawal tends to normalize disturbed cation relations because of the reduction of the sodium intake, foods so prepared are unpalatable and render lengthy application of such diets very difficult. Keining and Hopf therefore approached the problem from a new angle. Their experiments having shown them that the undesirable effects of common salt in the body are due to the sodium cation and not to the chlorine anion and bearing in mind that certain cations are antagonized by other cations, they sought to paralyze the undesirable sodium action by potassium, calcium and magnesium cations. From this standpoint they evolved a salt mixture which they term an equilibrated salt and which possesses approximately the same cation relation as that of the blood-serum and sea-water. Its formula is as follows:

Sodium .....	32.51%	Chloride .....	52.63%
Calcium . . . . .	1.42%	Lactate ....	3.79%
Magnesium . . . .	0.86%	Citrate .....	0.50%
Potassium . . . . .	2.7 %		

In order to test the correctness of the aforementioned theory Keining and Hopf carried out experimental and clinical studies in skin patients with various so-called sympathetic dermatoses. The first step was to show that such patients are sensitive toward sodium chloride. Accordingly eczema and urticaria patients were given sodium chloride by mouth which frequently caused marked exacerbation of symptoms following some days of salt-free nutrition. Unbearable itching usually resulted from this salt-flooding. When isotonic salt solution was injected wheals were produced at the injection site, while no wheals were obtained with an osmotically equilibrated glucose solution in the same patients. Next, the equilibrated salt mixture was injected and failed to produce wheals or caused only very feeble reactions in the same patients who had previously responded with wheals to isotonic salt solution injection. And when the mixture was exhibited orally for considerable periods in the same patients who showed exacer-

bated symptoms under sodium chloride flooding by mouth, no exacerbation of symptoms occurred.

Thereupon Keining and Hopf<sup>26</sup> treated various sympathetic dermatoses with a diet from which table salt was wholly excluded, but which was salted with the equilibrated salt. They lay claim to very good results in urticaria, eczema, erythema induratum, lichen, Duhring's, acne, tuberculides, lupus vulgaris and other skin conditions. Langer<sup>27</sup> has reported favorable results with this treatment in dermatoses, particularly in such as involved internal hypersensitiveness, but also in eczema, urticaria and pruritus, either alone or combined with local therapies. Schubert<sup>28</sup> made a study of the action of this electrolyte therapy in urticaria, pruritus, eczema, acne vulgaris and acne rosacea, neurodermatitis, hyperhidrosis, dyshidrosis and seborrhea. He concludes that the equilibrated salt diet plus simultaneous administration of an equilibrated potassium, calcium and magnesium mixture by mouth in tablet form or intramuscularly or intravenously, as recommended by Keining and Hopf, relieves or removes these conditions. This therapy tends to restore the body's normal cation relations and thereby conditions definite healing in numerous dermatoses. Bommer<sup>29</sup> has reported results with the Keining and Hopf equilibrated salt diet in 33 lupus vulgaris cases wherein the results were just as favorable as with the unsalted Herrmannsdorfer-Sauerbruch diet. He claims for the treatment the same curative effects as for the latter. In this country Eller and Rein<sup>30</sup> recently carried out a preliminary study of the equilibrated salt diet on 12 skin cases which included lichen planus, chronic eczemas of unknown etiology, urticaria, acne and lupus vulgaris. They observed exacerbation of symptoms under sodium chloride flooding in some of these cases with improvement under a diet free from table salt but which was salted with the equilibrated salt. In the lichen cases the intense pruritus almost entirely subsided and no new lesions appeared, though old lesions remained stationary. The urticaria patients and some of the eczema patients became free of symptoms. The authors suggest that the favorable response of the urticaria patients may be due to an influence of the diet on the calcium metabolism. The acne and lupus patients in this study did not respond to the treatment and the authors make allowance for the fact that while Keining and Hopf were able to hospitalize many of their cases this was not possible to them. They believe that the treatment represents a useful and valuable additional therapy in the treatment of selected dermatoses.

So far the equilibrated salt diet of Keining and Hopf has been studied chiefly in the field of dermatoses, including tuberculous skin affections. Its possible value in other forms of tuberculosis, including the pulmonary forms, remains to be determined.

Inasmuch as Keining and Hopf claim that the equilibrated salt, unlike table salt, does not cause water retention, they suggest its use in conditions such as subacute and chronic nephritis and also in cardiac and circulatory conditions. Further research is needed in this direction. If it were possible to employ a mixture which contains no less than 80 per cent. of sodium chloride in those conditions in which table salt is customarily avoided, without detriment to patients and without affecting the general action of salt-restricted diets it would unques-

tionably greatly facilitate their use and, as pointed out by Von Noorden,<sup>31</sup> would be of much service in dietetics.

### MECHANISM.

The mechanism of the Gerson and Herrmannsdorfer-Sauerbruch salt-restricted dietaries has so far escaped elucidation. The principles underlying the same involve the whole field of body chemistry and involve a change in the soil in which the tubercle bacillus grows. Many theories have been advanced, only a few of which can be dealt with here.

Grote<sup>32</sup> is of opinion that no adequate theory exists but favors the widely-held view that dehydration due to withdrawal of sodium chloride is the essential factor. This view is shared by Strauss.<sup>33</sup> Von Noorden<sup>34</sup> attaches great importance to the relative preponderance of the calcium-ion in the tissues which results from the reduced sodium intake. Bonner<sup>35</sup> believes that restriction of common salt and concurrent vitamin-rich feeding restores the functions of the capillary wall cells and that all other curative effects may be regarded as following from this action. He assumes that the vitamins do not unfold their full effects until the normal physiologic relations of the ionic environment of the vascular wall cells have been restored and that salt regulation and vitamin intake mutually support each other's action. Tesdal<sup>36</sup> has recently stated that he is inclined to ascribe the good results with the Gerson-Herrmannsdorfer-Sauerbruch diets in skin tuberculosis to more marked lactic acid production in the blood of patients with tuberculosis of the skin than in patients with pulmonary tuberculosis.

On the question of the dehydrating action of the diets Grote<sup>32</sup> draws an interesting analogy with the high altitude treatment of tuberculosis. He compares the mechanism of this therapy with that of the Gerson and Herrmannsdorfer-Sauerbruch diets and discerns a similar factor in both. The high altitude treatment acts independently of a specific dietary. Its active factor is the climatic one. The favorable results under it are obtained at all times of the year. But only one component of the entire climatic complex is constant and unaffected by seasonal or other periodic variations. It is the physiologic saturation deficit of the atmosphere, or, in other words, its unique dryness. All other factors, such as duration of sunshine, temperature, precipitation, etc., are inconstant when compared with the at all times demonstrable remarkable dryness of the air. The very high saturation deficit in these localities continually withdraws a maximum of fluid from the body by the respiratory route. The mechanism of this dehydrating action of high altitudes therefore resembles that of the salt-restricted dietaries. Grote makes the interesting suggestion that if the dietetic environment were adapted to the climatic one the therapeutic efficacy of both these measures might be increased, whereas we, at present, employ dietary and climatic therapies without reflecting that contradictions often arise between them which prevent the desired curative effect.

Herrmannsdorfer's claims that the Herrmannsdorfer-Sauerbruch diet shifts the tissue reaction to the acid side of equilibrium and that such a shift is desirable in tuberculosis have not found general acceptance.

Some authors found that the diet acidifies, others that it alkalizes. On this Herrmannsdorfer states that the action will depend on the nature of the preceding nutrition. Thus, if a strongly acid diet was given previously, the feebly acid character of the Herrmannsdorfer-Sauerbruch diet will cause a displacement toward the basic side, while with previous alkaline nutrition the diet will acidify.

The relationship between nutrition and acid-base equilibrium of the body involves two questions, *viz.*, whether a form of nutrition is capable of changing the existing acid-base equilibrium and whether such a changed equilibrium can influence other functional processes in the organism. True acidosis of the blood is impossible in the living organism. That which takes place in the blood during the occurrence of strongly acid products in the urine belongs wholly to the concept of compensated acidosis. Displacements among the carriers of basic and acid valencies take place frequently but never a displacement of the equilibrium. Only the urine and the expiratory air are influenced as regards their composition by acid or basic nutrition. The blood and the cells on the other hand are not freed from their constant environment by such nutritional changes. Notwithstanding this the internal displacement of ions is not without therapeutic importance.

The apparent contradiction that both acid and basic diet may dehydrate arises from the fact that the acidity of the urine and the relative basic or acid mixture of the individual radicles of the food do not influence the action of a diet. Such action is influenced solely by the mechanism of the specific ion action. An acid diet dehydrates because the acid radicles seize upon the body's fixed alkali depots and withdraw water from it owing to sodium impoverishment. In the case of strongly basic nutrition its anion poverty cannot cause retention of sodium in the body because it is itself sodium-poor and therefore unable to affect normal water elimination. Hence, while an acid action in a measure compels diuresis an alkaline action does not compel dehydration but merely permits it to take place.

### CONCLUSIONS.

In considering the theoretical foundations of the salt-restricted dietaries we find that individual dietary factors have been singled out as advantageous by certain workers and just as strongly denounced by others. Salt-restriction, low carbohydrate content, restriction of meat, high fat intake, special preparation of the foods to give a high vitamin content, have all been attacked and defended. In the face of existing uncertainties regarding the theoretical foundations it is clear therefore that any conclusions about the value of the salt-restricted therapies must rest largely on clinical experiments properly controlled over a long period.

There is a consensus of opinion that the diets bring about rapid and striking weight gains in most patients though parallel favorable influence on the pulmonary process is denied by many observers. Herrmannsdorfer has stated that weight gain under the diet is desirable only so long as the patient is undernourished and that the food intake should be reduced when normal weight is attained.

Despite the variations in the reported results with these diets many of their most violent opponents have admitted that this therapy signifies an advance. In 1931 I<sup>27</sup> reviewed the position of salt-restricted dietary in tuberculosis. It is my conviction that it represents a distinct therapeutic advance in the treatment of lupus vulgaris which is definitely curable by it. In regard to the opinion of various authors that the curative effects of the Gerson and Herrmannsdorfer-Sauerbruch diets are confined to lupus, Sauerbruch and Herrmannsdorfer take the view that the action of a nutrition which is capable of modifying the entire constitution cannot remain confined only to the skin and leave other organs wholly uninfluenced. This view would seem to receive support from some of the most recent researches which I have dealt with in this article.

Apart from my previously mentioned observations of the effects of the salt-restricted diets in pulmonary patients there have come under my observation cases of genito-urinary and bone and joint tuberculosis in which the diet helped to bring about favorable closure in an occasional sinus where other therapeutic procedures had failed for from one to two years, which was frequently accompanied by large gain in weight.

I believe the salt-restricted dietaries to represent an alternative therapy which is capable of raising the resistance of patients. Such an influence, even if partly psychologic, cannot be disregarded in the treatment of any form of tuberculosis. I believe this resistance-raising power of the dietaries in question to constitute the meritorious feature of these new and important dietary endeavors. Their striking effects may render necessary a reconsideration of the relative importance of the nutrition in the treatment of tuberculosis at least in particular cases.

If the accepted tuberculosis treatment represented the last word there would obviously be no need for contemplating new dietary or other procedures. That, however, is not the case. Every tuberculosis institution is faced by the non-response of some patients to the accepted therapies, of which the nutrition forms an integral part. Any additional assistance that can be obtained from the use of new dietetic measures would therefore prove extremely welcome.

Starting then with the assumption that the customary dietary measures do not constitute the final word we may ask ourselves what facilities exist for applying new dietary treatments which demand greater efforts than the customary nutrition.

As a general rule difficult dietary treatments are unpopular with many physicians. In institutions they are apt to cause serious dissensions which arise mainly from a lack of appreciation of the science of dietetics. This in turn is ascribable to insufficient attention to dietetics as a part of the student's medical curriculum. Recently Sir Walter Fletcher, Secretary to the Medical Research Council of Great Britain, in an address delivered in the United States, called attention to the lack of well-based and organized instruction in this field in Great Britain and greater attention to the therapeutic aspects of dietetics should be paid by practitioners and medical schools in this country. The elevation of dietetics from its present subordinate position, however, demands that the construction of tuberculosis institutions should conform to the needs. Many of these institutions are not provided with diet kitchens, without which no complex dietary treatment can



be carried through efficiently. Diet kitchens must also be properly designed and properly equipped. And as dietary treatments involve much special laboratory work that work must be carefully planned and carried through most conscientiously.

In *conclusion* we may say that although any schematisation of dietary therapies for all constitutions must be rejected, the results so far observed with the salt-restricted therapies indicate that dietary measures may hold formerly unsuspected therapeutic possibilities in tuberculosis. Further intensive research is needed to place them on firm foundations. But the growing tendency toward greater appreciation of the significance of the nutritional factor in the treatment of disease, which is manifesting itself in various quarters, is to be fervently welcomed by the profession as a whole.

TABLE I  
SHOWING CHIEF DIFFERENCES BETWEEN THE GERSON AND  
THE HERMANNSDORFER-SAUERBRUCH DIETS\*

	Gerson Diet	H.-S Diet
MEAT	At most 100 grams once a week	500 grams per week
Viscera	Prohibited	Permits spleen, liver, sweetbread, brain, lung, kidneys
Fish	Only about 70 grams per week	Permitted
Milk	½ pint daily	2½ pints daily
PROTEIN	Daily average about 40 grams	Daily average about 90 grams
Fat	Moderate amounts	160-200 grams daily
Cream	Prohibited	About ½ pint daily
Carbohydrate	Generous amounts	About 200-240 grams daily
Potatoes	Generous amounts	Not more than 125 grams per day
Eggs	Only yolk of eggs	Whole eggs
Raw Food	{ Predominant constituent of diet: 3-4½ pints of raw fruit juices and raw vegetable juices daily. . . . . }	{ Subordinate constituent of diet: 100 grams raw vegetable and 375 grams raw fruit daily. }

\*From *Kochbuch fuer Tuberkulose*, by A. and M. Hermannsdorfer, Julius Springer, Berlin, 1931.

TABLE II  
SHOWING PROHIBITED AND PERMITTED FOODS FOR THE GERSON DIET.\*

*Prohibited.*

- Table salt, in cooking and on the table.
- Soups.
- Canned goods of any kind.
- Pepper, mustard, vinegar, soup, spices.
- Salted and smoked meat (sausage, boiled and smoked ham, bacon, etc.).
- Salted and smoked fish, caviar, sardines, etc.
- Salted bread, cake, pastry.
- Chocolate, cocoa.
- Salted cheese.
- Sugar (about ¾ ounce per week permitted as a special concession for preparing particular dishes).
- Honey (about 2 ounces per week by special permission).
- Cream (except as an occasional addition to foods, ice cream or similar dishes).
- Alcohol (except Vermouth, Malaga, Cognac, on physician's prescription).

\*From *Grundsätzliche Anleitungen zur Gerson Diät*, M. Gerson, Muenchener Medizinische Wochenschr., 1930, 23.

TABLE II (Continued)

*Prohibited:*

- Tobacco (even a single cigarette is strictly prohibited).
- Coffee (except black coffee as a cardiac stimulant on physician's prescription).
- Tea (in intestinal disturbances Vermouth tea is permitted on physician's prescription).
- Carbonated water, mineral water, bottled lemonades.

*Obligatory.*

- Fruit, almonds, nuts.
- Vegetables, steamed in their own juices with fresh butter or fresh olive oil, and prepared without sugar or flour, 1 to 2 times daily.
- Leaf salads, tomatoes, etc., as desired, without vinegar.
- Raw egg yolk, 2 to 3 daily best taken with lemon and orange juice.
- Raw vegetable juice, prepared as directed, chilled, to be sipped very slowly, commencing with 3 glasses and increasing gradually to 6 to 8 glasses daily.
- Fruit juices (raw), 3 glasses daily.

*Permitted.*

- Milk 1 glass (200 c.c.) daily. Preferably buttermilk, kefir or Yoghurt.
- Flour, rice, farina, etc.: Not more than 35 grams flour, 50 grams rice and 50 grams farina per week.
- Meat and fish Of each once a week as a special concession. The physician may prescribe 2 to 3 smaller portions instead of one large one of 100 grams, in severe cases or may prohibit meat or fish entirely. These quantities may not be exceeded except in special cases.
- Potatoes. Need not be restricted except in obesity or with too rapid gain of weight. They should be eaten with the jacket at least three times a week. In obesity, etc., they should be restricted to 200 grams.
- Bread: Salt-free whole wheat or salt-free whole rye. 40 to 80 grams daily as directed by the physician. Patients performing physical labor may receive a little more.
- Oatmeal: 40 grams oatmeal gruel with 10 grams butter 1 to 2 times daily. The physician will either permit or prohibit it.
- Puddings, egg dishes, desserts, ice cream: According to physician's prescription directions on an average once a week in portions of about 100 grams.
- Cottage cheese: On physician's prescription 10 to 50 grams daily, but prohibited on strict days.
- Seasonings. Liberal use of the following: marjoram, tarragon, dill, onions, peppermint, bay-leaf, scallion, caraway, parsley, celery, garlic, ginger, vanilla, cinnamon, anise, currants, almonds, coconut, nuts, raisins, leek, lemons, horseradish, black radish, radishes, olive oil.
- Alcohol: Only for flavoring foods, Malaga, Vermouth, Claret, home-made fruit syrups and fruit wines.
- Coffee, tea, cocoa. Only for coloring the milk.

TABLE III

## SPECIMEN DAY'S MENU FOR THE GERSON DIET.

*Morning Nourishment:*

- Oatmeal gruel (not strained) with much butter and some vegetable or fruit juice.

9 A. M.

- 2 to 3 raw egg yolks with lemon.
- Grated black radish, tomato or fruit.
- 30 grams cottage cheese.

TABLE III (Continued)

*Dinner:*

Vegetable pudding with horseradish sauce.  
 Beets (steamed).  
 Mashed potatoes.  
 Salad and grated carrots.  
 Caramel cream.

*4 P. M.*

½ pint uncooked milk.

*Supper:*

Steamed tomatoes.  
 Rice.  
 Lettuce.  
 Fruit.

*Night Nourishment:*

Oatmeal gruel with much butter and little vegetable or fruit juice.

The raw vegetable juices are prepared from spinach, carrots, beets, kohlrabi, oyster plant, tomatoes, apples, celery, leek, mixed in certain proportions. Taken in oatmeal gruel and alone throughout the day.

The fruit juices are prepared from lemons, oranges, or grapes or apples. Taken throughout the day.

TABLE IV

SHOWING PROHIBITED AND PERMITTED FOODS FOR THE  
 HERRMANNSDORFER-SAUERBRUCH DIET.

*Prohibited:*

Table salt.  
 Canned foods of any kind.  
 Smoked or spiced meat (sausage, boiled ham, bacon, corned beef, etc.).  
 Smoked or pickled fish.  
 Bouillon cubes, meat extracts, except those given under Permitted Foods.  
 Salt butter.  
 Ordinary bread.  
 Soda crackers or other salted crackers.  
 Cheese, except home-made cottage cheese or commercial salt-free cheese.  
 Shrimps.  
 Alcohol, except for flavoring foods.  
 Water, as a beverage.

*Permitted:*

Vegetables (raw, steamed, and as salads): tomatoes, carrots, oyster plant, kohlrabi, leek, beets, asparagus, cauliflower, red cabbage, white cabbage, savoy cabbage, Brussels sprouts, cress, endive, lettuce, rhubarb, sorrel, spinach, peas, string beans, lima beans, lentils, mushrooms, cucumber, egg plant, chicory.  
 Fruit: All kinds of raw fruit, also stewed and dried fruit like dates, figs, muscatels, sultanas, currants.

Nuts: Chestnuts, Brazil, pecans, walnuts, almonds, and any other unsalted nuts.

Jams, Jellies, Marmalades: Home-made.

Milk: Raw, if source first-class, otherwise pasteurized uncooked. Also sour milk, buttermilk, kefir, Yoghurt.

Cream.

TABLE IV (Continued)

*Permitted:*

Cheese: Cottage cheese (home-made), Yoghurt cheese, commercial salt-poor cheese, imported Parmesan cheese (home-grated and used only occasionally in extremely small amount as it contains 1.3 to 1.6% table salt).

Eggs: Alone and also in mayonnaise, gravies, puddings, creams, soups, etc.

Fats: Sweet dairy butter (salt-free), olive oil, salt-free hog's lard.

Meat: All kinds of fresh meat.

Viscera: Spleen, liver, sweetbread, brain, lung, kidney.

Fish: All kinds of fresh fish.

Potatoes: Not more than 4 ounces per day.

Bread: Salt-free whole wheat or salt-free whole rye, Zwieback.

Flour: For pastries and gravies.

Noodles, Macaroni: Home-made

Rice: Brown rice only.

Cereals: For steaming or cooking, such as oatmeal, cream of wheat, hominy, barley, brown rice, wheatena. Ready cooked cereals like cornflakes, etc., to be avoided.

Sugar: Brown sugar preferable, also white sugar.

Honey: Genuine bee's honey.

Coffee, Tea, Cocoa: To be used in small amounts only for coloring the milk.

Herbal Teas: Like lime blossom, camomile, peppermint, etc.

Apple Cider: Sweet cider only, not more than half a glass twice a week.

Beer: Alcohol-poor beer, 1 small glass three times weekly.

Seasonings: Marjoram, tarragon, dill, peppermint, chervil, onions, leek, capers, bay-leaf, juniper berries, scallion, caraway, lemons, parsley, sage, rosemary, basil, fresh cayenne pepper, celery, garlic, horseradish (home-grated), radishes, black radish, soup roots, nutmeg, nutmeg blossom, ginger, vanilla, cinnamon, anise, currants, almonds, cocoanut, brazil nuts, raisins, mustard, vinegar. Pepper and mustard to be used in very small amount. Worcester sauce (only Lea & Perrins) to be used only very exceptionally in *smallest amount*. Lemco (meat extract) contains table salt and is to be used only rarely in *smallest amounts*.

Salt Substitutes: Eugusal, bromhosal, to be used *very sparingly*. Also eugubrol, citrofin-salt.

Wines, Liqueurs, Spirits: Only for flavoring foods.

TABLE V

## SPECIMEN DAY'S MENU FOR THE HERMANNSDORFER-SAUERBRUCH DIET.

## 7 A. M. (Morning Nourishment):

Milk soup (milk, oatmeal, butter, half egg yolk raw, sugar). Followed by cod-liver oil,  $1\frac{1}{2}$  tablespoons.

## 9 A. M. (Breakfast):

Weak Coffee (coffee substitute or very little coffee bean) with much milk; or tea or cocoa with much milk.

Bread with butter or jam or honey.

Raw Vegetable (carrot, cauliflower, cucumber, celery, radishes, tomatoes, green peas etc.) Followed by a mineral mixture (calcium).

## 10 A. M. Fruit Juice.

TABLE V (Continued)

## 12 P. M. (Dinner):

Tomato soup (1 small cup).  
 Roast beef.  
 String beans (steamed).  
 Potatoes steamed in jacket.  
 Lettuce and cucumber salad.  
 Grape fruit.

Followed by a mineral mixture (calcium)

## 3 P. M. (Afternoon Nourishment):

Cream (if desired with a little tea or coffee), zwieback or cookie or bread with butter or jam or honey.

## 5.30 P. M. (Supper):

Egg with mustard sauce.  
 Bread and butter.  
 Raw celery.

Followed by a mineral mixture (calcium).

## 8 P. M. (Night Nourishment)

Milk soup (milk, cream of wheat, half egg yolk, butter, sugar). Followed by cod-liver oil, 1½ tablespoons.

TABLE VI

SHOWING DAILY QUANTITIES OF THE PRINCIPAL FOODS FOR A  
 PATIENT WEIGHING ABOUT 132 POUNDS

## Foods:

Salad and Vegetable	200 Grams
Raw Vegetable	100 Grams
Fruit . . . . .	375 Grams
Fat (butter, oil, etc.).	100 Grams
Milk . . . . .	1250 Grams
Cream . . . . .	100 Grams
Egg . . . . .	One to one-and-a-half
Meat, Viscera, Fish. . . . .	70 Grams
Potatoes . . . . .	125 Grams
Bread . . . . .	60 Grams
Zwieback or Cookie. . . . .	20 Grams
Starch (flour, rice, farina, oatmeal, etc.) . . . . .	30 Grams
Sugar or Honey . . . . .	30 Grams

Containing about 90 grams protein, 164 grams fat, 244 grams carbohydrate, with total calories 2886 and about 3.4 grams sodium chloride.

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## CHAPTER XVIII.

# MEDICINAL, SYMPTOMATIC AND TUBERCULIN THERAPY.

BENJAMIN GOLDBERG

### SPECIFIC THERAPY.

There has been no successful specific devised for the treatment of tuberculosis. As a result thousands of therapeutic agents have been recommended and have passed on into oblivion. This has necessitated the present therapeutic systematization, based on those factors which our present immunologic and pathologic knowledge has dictated.

Concerning the value of specific chemicals, medical history contains many references to the use of these, particularly metals and metallic salts, in the attempted treatment and control of various diseases by healers throughout ancient and medieval times. *Chemotherapy* in tuberculosis, however, received its great stimulus as the result of the achievements of Paul Ehrlich in the development of arsenicals for the successful treatment of trypanosomatic diseases. As a result of this work, investigators in the field of tuberculosis therapy attempted three types of research. These involved, *first*, the introduction of bactericidal substances into the body through direct injection into the blood stream, absorption into the blood stream after subcutaneous injection or by gastrointestinal feeding, or through absorption in the respiratory tract, utilizing chemicals in combination with inhalants.

These methods all aimed at the destruction of the tubercle bacillus *in vivo*, without destruction of the body tissue cells in and surrounding the disease area. Jaffé has shown that only "in very few instances do blood-vessels penetrate tubercle," and, therefore, with blood-vessels thrombosed in the periphery of areas of tuberculous pathology, direct action upon the bacilli in the caseous centers *through the application of such therapeutic agents has limited possibilities.*

The second mode in the utilization of bactericidal substances in chemotherapy is based on their combination with aniline dyes in the hope that a chemotactic cellular affinity for such dyes would take place and allow bacillary destruction.

**Sulfonamides and Sulfones.**—*Diasone, Promin and Promizole.*—The striking results which were obtained with sulfanilamide in a group of bacterial infections interested Rich and Follis<sup>10</sup> in exploring the possibilities of this drug in experimental tuberculosis. The inhibitory effect observed in experimental tuberculosis in guinea pigs stimulated a group of other workers into utilizing the same and other similar new chemical compounds in the hope of finding one which might prove effectual in tuberculosis. The substances which have been used have belonged to the sulfonamide and sulfone group of chemical compounds, which have undergone synthesis in the chemical laboratories in fairly rapid sequence during the past several years. *Conflicting statements as to the efficacy of some*

of these compounds have come with the reports of different experiments conducted by the different investigators involved in this work. The varying effects reported seem to be related with the alteration of the original chemical in the production of the new compound, the toxicity of the substance, the dosage, the time of utilization of the compound in reference to the inoculation of animals with the tubercle bacillus and the development of the disease. And also the maintenance of concentration in the body as affected by the dosage used and the oral or parenteral introduction of the chemical.

Animal experimentation has shown that there is a definite inhibitory and bactericidal action in some of these new chemical compounds. The investigative work of Smith, *et al*.;<sup>20</sup> Callomon;<sup>21</sup> Feldman and Hinshaw;<sup>22</sup> *et al*.; Buttle and Parish;<sup>23</sup> Raiziss, *et al*.;<sup>24</sup> has yielded information as to which compounds might be valuable in coping with tuberculous infection. Following the basic and controlling experiments, two chemical compounds, namely, Diasone, first prepared by Raiziss in December, 1937, which is the name given to disodium formaldehyde sulfoxylate diaminodiphenylsulfone; and Promin, which is sodium p,p'-diaminodiphenylsulfone-N,N'-dioxetane sulfonate, were determined to be of value in destroying the tubercle bacillus in guinea pigs experimentally inoculated. Both of these compounds have a relatively high toxicity, however, not only for guinea pigs, but as later evidenced in human beings.

Petter and Prenzlau,<sup>25</sup> reporting on the use of Diasone in 44 of 100 patients who had received it at their institution, said that in pulmonary as well as in extrapulmonary lesions improvement was evidenced in most of the patients, and in the pulmonary cases no instances of bronchogenic dissemination were observed during the period of chemotherapy. Yet all patients did not improve, and it is their feeling that this substance is as yet not the ideal one to utilize as a specific in tuberculosis but rather as an adjunct therapeutic agent. In the selection of their cases, they discussed the first group as having only infiltrative lesions, without cavitation. But, apparently, later these cases have either progressed to cavitation and were therefore not simple infiltrative lesions, or new cases with cavitation were added to the treatment group. In discussing results in their series, emphasis is placed upon the results in what can only be caseous pneumonic tuberculosis.

Dancey, Schmidt and Wilkie,<sup>26</sup> reporting on a series of 27 patients with pulmonary tuberculosis in which Promin was used, selected patients with advanced disease, supposedly with a poor prognosis. They also did not adhere to a pathological classification which would more positively identify the exact type and extent of pathological lesion in these patients. It would seem that their thought was to determine the effectiveness of Promin in destroying tubercle bacilli in the human being. They, too, stress the importance of careful clinical supervision during the administration of the drug, because of the toxic reactions that they have observed, and conclude that the "curative action" of Promin in human pulmonary tuberculosis is not very potent and Promin alone should not be relied upon to effect an arrest in any case.

Hinshaw, Pfuetze and Feldman,<sup>27</sup> reporting on the treatment, with Promin, in a series of 36 patients out of a total group of 106 who had received this chemical,



also conclude that as yet the sulfone series of chemicals have not yielded positive evidence of healing in a sufficient number of cases to recommend the drug as a specific. While at this time most of the untoward manifestations arising as a result of the toxic effects of the chemical can be controlled, the greater benefits observed were in those cases of pulmonary disease of an exudative type, with an extensive demonstration of tissue fibrosis. Promizole, which is the 4,2'-diaminophenyl-5-thiazolesulfone, is more recently being utilized by these workers, and this chemical shows less toxic manifestations in higher dosage, but at this writing sufficient evidence has not been accumulated to report the effect on human beings with tuberculosis.

In their more recent report Hinshaw, *et al.*,<sup>28</sup> in a further progress report of the 36 patients who were originally placed on Promin, state that those who very early showed evidences of improvement have in most instances continued such improvement. In several of the cases the arrest of disease was obtained through adjunct collapse therapy. Those that only showed slight improvement, or no improvement, have mostly shown progressive disease. This, despite the fact that all the patients received relatively large doses of Promin. Again this investigating group places emphasis on the fact that "exudative lesions of recent origin appear to be more promising types for chemotherapy than those which involve caseation, necrosis, cavitation and fibrosis."

The benefits that seem possible in the human through the application of one of these drugs, or a new compound which may result from the studies of these chemicals, may be stated as follows: The possibility of a bactericidal action which will in the introduction of the new chemical destroy any or all tubercle bacilli which have invaded the human body. This should include the organisms and pathological concomitants seen in the primary tuberculous focus, or in new or old hematogenous or lymphogenous distribution of tubercle, or in the new bronchial spillover from caseous pneumonic tuberculous disease. Greater difficulty might be envisioned in the presence of cavities unless secretion of the drug is possible through cavity walls highly vascularized. In other instances of cavity formation, endobronchial insufflation might allow sufficient bactericidal action. Topical applications of the drug either in powder or in ointment base or even in solution might prove of benefit in endobronchial lesions as well as other accessible and even directly inaccessible ulcerative tuberculous processes. In reviewing the studies which have involved human beings, there has, as is very commonly seen in such research, been a failure to carefully classify the various pathological types of pulmonary tuberculous lesions. Thus one does not readily distinguish between those exudative processes, which would have healed spontaneously when only protected from new superinfection, as against the more serious caseous pneumonic types with cavitation as the dominating picture.

The eradication of cavitation, even after destruction of organisms, remains in most instances a mechanical problem. We still look forward with an intense interest to continuation of this type of research, and hope that the chemical effective in eradicating tuberculosis from the human host will soon be available.

Other substances of a chemical nature have been introduced into the body to increase phagocytosis in and about the diseased area and to stimulate the fixed tissue cells. This was done to create more granulation tissue, which, as it became fibrotic, would limit the lesion at its periphery and tend to prevent extension of the pathology.

**Metallic Salts, Gold.**—The metallic salts have been utilized experimentally as therapeutic agents in tuberculosis for many centuries. The outstanding experiments in this field deal at this time with a gold preparation, Sanocrysin, which is an inorganic salt of gold. A double thiosulphate and sodium with gold in a trivalent form, has been recommended by Möllgaard for the active treatment of this disease. Many conflicting reports have come into the literature since this investigator reported success in its use. Complications of a serious type, particularly an involvement of the kidneys, have been reported by competent observers. Personally I have seen a series of individuals who have had this form of therapy and in whom there was definite evidence of kidney disease, manifested by a decrease in the renal permeability, as depicted in the blood chemistry and kidney functional tests as well as in the urinary findings.

Amberson, McMahon and Pinner<sup>1</sup> have also reported on the various dangers incidental to the use of this substance. Recent reports emanating from the Continent, seem to take a more favorable light on the use of sanocrysin. A study of these reports shows that no attempt has been made to segregate the pathologic types of the disease so that one might have information as to whether the beneficial results reported occurred in the malignant, serious caseous pneumonic group, or were merely the natural healing that occurs almost spontaneously in the benign exudative types of disease. We would, therefore, withhold any recommendation for the use of this substance and other similar compounds until more adequate data concerning its utilization can be established in preventing the serious complications that we have met.

Many other substances such as dyes, oils, metals and their salts have been used therapeutically in tuberculosis without avail.

**Calcium.**—The utilization of calcium as a therapeutic agent in the treatment of tuberculosis has been based for many years on the supposed demineralization theory. Many writers reported an excess of calcium salts in the urinary and alimentary excreta in the presence of active tuberculous disease and therefore felt it was necessary to replenish the body tissues. In discussing calcium, we do not lose sight of the other mineral salts (phosphorus, etc.) which have important parts in body function, yet are little understood.

In recent years considerable experimentation in this field has given rise to many new ideas as to the value of this substance. Many investigators have attempted through feeding calcium or calcium compounds to increase the deposition of lime salts into areas of tuberculous disease in the hope of creating calcification which would result in healing. This only occurs in a very small proportion of patients with the disease. It seems, however, that at the present time there is a definite understanding that an increased calcium intake in itself does not affect the blood or tissue calcium unless certain activating substances

are present to aid in the tissue deposition of calcium with a consequent increase in its absorption.

The studies in tuberculosis that relate to calcium have resulted in some more or less definite conclusions. Peterson and Levinson<sup>2</sup> have reported more deaths among tuberculous patients with a low blood calcium. Those patients with a higher blood calcium evidenced a healed or healing lesion and, therefore, a good prognosis. There were, however, instances in their series in which a high blood calcium was found, associated with an advanced lesion, which change these investigators attribute as due to a transfer of the calcium from disintegrated tissue to the blood.

Cantarow reports that in a series of patients with a chronic fibroid tuberculosis a considerable variation in respect to the diffusibility of the serum calcium was present; an increased diffusibility in active exudative cases; and a decreased diffusibility in benign proliferative types. Cantarow,<sup>3</sup> also in studying the diffusible calcium ratio in sixteen patients having advanced exudative lesions, all clinically active, four of which patients were critically ill, demonstrated a diffusibility ratio of 117 to 152, the ratio in normal, healthy individuals being 82 to 115.

In a series of eleven individuals with fibroid tuberculosis, none of whom were critically ill, the diffusibility ratio varied from 56.7 to 80.1. Thirty-six patients showed a normal range—82 to 115—these latter all having chronic ulcerative tuberculosis in varying stages of activity. In this latter group there appeared to be no correlation between calcium distribution and the nature or extent of the pulmonary lesion. Increased diffusibility of blood calcium denotes increased permeability and it appears that an increased ratio of diffused to non-diffused calcium is associated with the exudative types of tuberculosis, while a subnormal diffusibility ratio occurs in proliferative or fibroid tuberculosis.

Peterson,<sup>4</sup> with his "blister test" shows the presence of diminished permeability through the skin capillaries in fibroid tuberculosis, but in the exudative types of the disease the permeability seems to be definitely increased.

Wolf<sup>5</sup> reports a temporary rise in the leukocytes, following an increased calcium intake, and while she states the questionable value of this change, she suggests a possible benefit through increased phagocytosis in this disease.

One might also mention the work of Ellman,<sup>6</sup> who recognizing the place of the parathyroid gland secretions in calcium metabolism in the body, studied the histologic structure of such glands in the tuberculous and noted evidence of increased function in such tissue sections, which would, according to this worker, depict the need for an increased calcium intake.

The work of Peterson and Levinson<sup>2</sup> in capillary permeability, and my personal work with Reed, has led me to feel that calcium is important and that its value in tissue reactivity is to stabilize tissue cells and to control the phenomenon of sensitization or allergy. In tuberculosis this may be summed up as follows:

Initial or primary infection in the human host creates a sensitization or reactivity of tissue to further infection with tubercle bacilli. This sensitization

or reactivity is manifested in its most minute form by cell irritability, which when marked, allows of increased cell permeability and, therefore, increased capillary permeability. A new infection with tubercle bacilli, usually exogenous in origin, stimulates this sensitization procedure so that exudate is poured out as a result of cell irritability and permeability. Such exudate may either fix the bacilli *in situ* or may also be an attempt on the part of nature to wash these irritating bacilli from the tissue cells where they have settled.

This is normally considered a defense reaction on the part of tissue cells in the presence of organisms which may propagate, but where extensive exudate is thrown out and carries bacilli invading new tissue, it may create new pathological entities and endanger the patient. The degree of tissue reactivity and capillary permeability, resulting from the irritation of the infecting organism, is dependent upon the irritability of the single cells and the permeability manifested by such cells. An increase in the calcium content of the body tissues and blood apparently tends to lessen cell irritability and capillary permeability, thereby lessening the amount of exudate, hardening, as it were, the fixed tissue cells, preventing an extension of the infecting organisms and tending to limit the destruction by their toxins.

The improvement of calcium metabolism in the body seems to be largely dependent upon certain specific, activating substances, of which the most important, to our knowledge at this time, is vitamin D. Before discussing the rôle of vitamin D, I would mention other associated conditions which affect this metabolism.

When taken into the body by the alimentary tract, calcium absorption is based on several factors. The hydrogen ion concentration of the small bowel is important, inasmuch as an alkaline medium tends to cause insoluble calcium salts. Kahn and Roe<sup>7</sup> have shown adequate absorption in calcium feeding when calcium is given between meals, at which time intestinal alkalinity is not so marked. Bernheim<sup>8</sup> states that the fats may, through combination with calcium, form insoluble soaps, and oxalic acid in some vegetables may form insoluble calcium oxalates. An excess of phosphorus in proportion to calcium may also form an insoluble tertiary calcium phosphate. Bergeim<sup>9</sup> demonstrated increased calcium and phosphorus absorption in the presence of calcium lactose feeding because of increased acidity, due to lactic acid fermentation. Mellanby<sup>10</sup> has determined that decreases in calcium and phosphorus absorption occur with quantities of bread, oatmeal, maize and rice in the diet. It would, therefore, seem important to heed these results of experimentation in calcium feeding.

The amount of calcium to be given and the type of calcium has created controversial discussion. It seems wise in the light of recent work on the importance of phosphorus in conditions where a deranged calcium metabolism is the most prominent clinical feature, to administer calcium in combination with phosphorus. This is warranted on the basis that a large dietary excess of phosphorus inhibits adequate absorption of calcium, and may even draw on the calcium or fixed base reserves of the body, resulting in a negative calcium balance; likewise a large excess of dietary calcium may be expected to combine with phosphorus, drawing it from the body stores, and resulting in its excretion

as calcium phosphate. It is by thus feeding a large excess of calcium as compared to phosphorus that rickets is experimentally produced. For this reason it seems advisable not to use routinely the organic salts of calcium, as the lactate or gluconate, but preferably one of the calcium phosphates. Powdered bone meal, essentially tricalcium phosphate, is available commercially; I have used a mixture of this material with dicalcium phosphate. The advantage of using such inorganic preparations is that calcium and phosphorus are supplied in approximately the same proportion as is required for the calcification of tubercles. Calcium gluconate and lactate may be given for immediate emergency. The dosage should be from .10 to 20 grains three times daily to supply evident needs or dietary deficiencies.

**Vitamin D.**—The efficiency of calcium metabolism is apparently dependent upon the presence of certain conditions in the body, as pointed out above, in addition to the presence of activating substances, of which vitamin D at this time stands out as most important. We would not here delete the thought that some of the other vitamin substances may and do act as synergists in stabilizing the mineral metabolism of the body.

The research of Mellanby,<sup>11</sup> of Hess,<sup>12</sup> and of McCollum<sup>13</sup> pointed the discovery of vitamin D in foodstuffs, as did Huldshinsky<sup>14</sup> with ultraviolet light, in determining its anti-rachitic value. This anti-rachitic action is dependent upon changes in the calcium and phosphorus chemistry of the body. Recent experimentation as to the value of vitamin D has been extended to other disease syndromes, particularly the sensitization or allergic group of diseases.

Vitamin D, in sufficient quantities, has the ability to mobilize calcium in the blood, acting singly or possibly through the parathyroid hormone. It thus, if given in adequate amounts, may produce a hypercalcemia with increased deposition of calcium into tissue cells, and a resulting increased calcium absorption. This complex mechanism of biochemical activity influences cell and capillary permeability and, therefore, exudative processes which are factors in cell reactivity, sensitization or allergy.

1. *Cod-liver Oil.*—This oil has been used empirically for many centuries in the treatment of pulmonary tuberculosis without any definite knowledge of its action. More recently, with the extension of knowledge of vitamins, has come a realization of its importance in the maintenance of the mineral metabolism in the body through its vitamin D content. In addition, it has a liberal vitamin A content, traces of iodine, biliary salts and other substances, which latter group are all of questionable additional value. The fat content is of importance as a food in the patient of poor nutrition. Preference is given to cod-liver oil in vitamin D feeding in the general diet of the tuberculous. Cod-liver oil here is given in amounts of one-half to one ounce three times daily after meals. The cod-liver oil selected for use should be one of the products of a reputable manufacturing concern with adequate testing facilities. Where obesity is present, or additional vitamin D is necessary, a fortified preparation containing viosterol may be utilized, so that smaller amounts of the oil may be given, yet dispensing an adequate amount of vitamin D. In such instances cod-liver oil 10-D is given in amounts of 1 to 2 teaspoonfuls after meals. Where personal distaste to the oil is present.

it may be given in such vehicles as orange juice, tomato juice, wine, etc. Even in such vehicles patients may manifest digestive upsets or may have other idiosyncrasies and refuse to take this important substance. Vitamin D may then be given in the form of irradiated ergosterol (viosterol).

2. *Viosterol*.—Applying the knowledge that ultraviolet rays had an anti-rachitic factor, Hess and Anderson<sup>15</sup> and Griffith and Spence<sup>16</sup> have shown that the wave lengths most potent in developing this substance existed in the ultraviolet zone between 302 and 265 millimicrons. Irradiation of ergosterol with ultraviolet produces a substance which may have a potency as regards the anti-rachitic element ranging from 200,000 to 700,000 times that in the average cod-liver oil, making necessary dilutions to the potency of 100 times the standard cod-liver oil, which is the common commercial preparation. The work of Bills in the Mead-Johnson Company laboratories has been most important in improving the preparation of viosterol and its diluents.

The dosage of viosterol which we previously used has approximated 15 to 20 drops, using the dropper furnished when the product is purchased. At present larger doses are recommended and these doses may approximate 5 to 10 times the former dosage. Preparations of greater concentration are now on the market.

**Creosote and Guaiacol.**—These substances and their various derivatives have been recommended in the treatment of tuberculosis for a century. There is no definite evidence of any beneficial effect they may have on tuberculous pathology. They do, however, seem to exert a mild inhibitory reaction on the super-imposed inflammatory process produced by secondary infections. They may thus, through decreasing the secretions of such secondary infections, lessen the possibility of spread of tuberculous infection, limiting the "spilling-over" process of infected secretory material. Their use is therefore recommended under such conditions, especially where an irritative cough is present, associated with abundant sputum. While some phthisiotherapists recommend their use to stimulate the appetite and digestion, we feel such improvement results from the lessened respiratory tract toxemia. There is, however, a definite tendency for this medicament to produce gastric upsets. When this occurs, or in the presence of a protracted febrile course, in the presence of hemoptysis or kidney irritation, evidenced by albuminuria, its use should be discontinued. Beechwood creosote may be used in amounts of 10 to 20 minims added to 4 ounces of a simple cough mixture, such as:

<i>R Beechwood Creosote</i> .....	0.65
<i>Syrupi scilla</i> .....	100
<i>Syrupi tolu</i> .....	200
<i>Syrupi pinus alba</i> .....	70.0
<i>Aqua q. s. ad.</i> .....	120.0

M. S. Shake and take 1 teaspoonful every four hours.

Creosote carbonate in 5 minim doses, floated on milk or taken in capsule is not disagreeable. Equal parts of creosote and alcohol may be used as an inhalation or may be instilled directly into the trachea where a severe irritative cough is present.

Guaiacol is used principally as syrup of potassium guaiacol sulphonate, which is palatable, except to a few individuals who have an idiosyncrasy to it. This syrup may be given in 1, 2 or 3 dram doses in water at three- or four-hour intervals.

**Iodine.**—This substance has been used in the form of its alkaline salts, the sodium or potassium, or as the tincture or Lugol's solution which contains these salts in addition to iodine. The use of the alkaline iodine salts in the exudative or caseous pneumonic lesions causes an increase in the blood supply in and about the site of the tuberculous disease. This increases the secretions in this area and tends to break down and carry necrotic tissue from the area of tuberculous disease into the bronchial tract. It thus allows a "spilling over" of tuberculous infection into uninvolved tissue. It is this action of the iodide salts which for many years, as a diagnostic procedure, was used to produce sputum containing tubercle bacilli, where a questionable tuberculosis existed. This procedure is to be condemned and never employed. Extension of tuberculous disease and hemoptysis have been encountered in many instances following its use. Employing iodine in tuberculosis for a number of years, we have used a solution of iodine, in glycerin and alcohol, as below:

Iodine resublimed	.... .	90 0
Alcohol 95%	.. . .	400 0
Glycerine	.....	500 0
Allow to stand for 2 weeks.		

This is without the addition of the iodide salts. No deleterious results have been seen from this solution, even in exudative cases where it has been used to treat, or as a diagnostic aid in associated thyrotoxicosis. Iodine is used in pleurisy, especially with effusion, and in some instances of chronic fibroid or the scirrhus type of pulmonary disease, which frequently have associated asthmatic manifestations. The average dose of 10 minims of the above solution may be given in milk three times daily and increased, if necessary, or if symptoms of iodism appear, to as high as 30 to 60 minims three times daily in a glass of milk, preferably after meals.

**Liver Extract, Iron and Copper.**—Secondary anemia is very frequently found in tuberculosis. It is usually the result of the chronic toxemia incidental to the disease, as well as the loss of appetite seen in the majority of tuberculous individuals. In some instances idiosyncrasies are present to those foodstuffs which engender blood building, so that there may be an impoverishment of those important substances. Not infrequently do we meet individuals who have idiosyncrasies to important foods, such as rare meats, egg-yolks, liver, etc. Where such idiosyncrasies exist, or in the presence of a blood condition which requires more rapid upbuilding, it may be necessary to use concentrates which will overcome this condition.

Whipple<sup>17</sup> in 1925 and Minot and Murphy<sup>18</sup> in 1926 began and stimulated the use of liver therapy in anemia. Since their original work, considerable research has been done and valuable information has resulted in the combating of both the primary and secondary forms of anemia. More recently Steenbock

and his associates at the University of Wisconsin have demonstrated the importance of *copper* as an activating substance, along with the feeding of iron and liver, in overcoming some of the blood dyscrasias. The high caloric, high vitamin diet, which is given in the chapter on that subject, contains an adequate amount of the various substances necessary to maintain blood stability, but in the presence of anemia, to more rapidly overcome this manifestation, it has been our habit to utilize one or other of the several preparations containing these ingredients in adequate amounts. In addition to the substances mentioned above, the liver or its extracts apparently contain other important ingredients which have not as yet been determined.

### TREATMENT OF SYMPTOMS.

Symptoms that occur in pulmonary tuberculosis are produced by mechanical irritation, cough, sputum, hemorrhage, or are the result of the toxemia produced by an active disease process and may be listed as fever, tachycardia, night sweats, anorexia, dyspnea, etc. Both groups of symptomatic manifestations require the usual therapeutic régime of adequate rest in all of its details and the practitioner should insist upon most careful adherence to the establishment and maintenance of proper surroundings for the patient as well as fresh air and proper foodstuffs.

1. *Fever*.—Fever is an indication of toxemia resulting either from an active pulmonary lesion or some complication. Its presence indicates the necessity for definitely determining the presence or absence of such complication. Adequate treatment for its control or removal must be rendered when such complication is present. Where the activity of the pulmonary lesion is the causative factor, general rest is the most important indication. The patient should be kept in a well aerated room and absolute quietude be observed. A state of mental depression may sometimes effect a febrile rise. A change of environment, even temporarily, may produce an euphoria that seems to alter the reaction of the patient, producing a curtailment of toxemia and lowering of temperature.

Collapse therapy is the ideal way of controlling temperature, due to pulmonary tuberculosis, where the indications permit, the type of collapse being determined by the pathology present.

The prone position, frequently advised by some therapists, may be responsible for toxin absorption. Placing the patient in a semi-recumbent position, through the use of additional pillows or a back rest, may alter the drainage through the respiratory tract and lessen such absorption and fever.

Hydrotherapy, as a tepid sponge bath or light alcohol rub, is very refreshing to the patient and should be a matter of routine. In patients having non-tuberculous respiratory infections, coal-tar products, combined as follows, may be used:

R <i>Acid. acetylsalicylicæ</i> . . . . .	gr. iij
<i>Acetphenetidini</i> . . . . .	gr. iij
<i>Caffeine citratis</i> . . . . .	gr. i

M.S.—In capsules. One every three or four hours

This formula I also use in those conditions where hyperpyrexia creates a need for temporary aid. In the carefully supervised patients only rarely have



I found use for additional antipyretics. The dietetic management of patients in a febrile state is considered in the chapter on Diet.

2. **Night Sweats.**—This symptom is the result of a severe toxemia produced by the tuberculous process or by secondary invaders. It is best controlled by a careful adherence to all of the details of the general management of the patient, which deal with the subsidence of disease activity. In patients with less extensive pathology, it may disappear almost immediately on complete general rest in a favorable environment. Even in the presence of more extensive disease, it may be alleviated by careful supervision of detail to rest, ventilation, and particularly to the amount and weight of the bed clothes. In many of the instances where it has continued, the bed clothes were found to be a causative factor. The only medicament we have found to be of value, and that only temporarily, is atropin in doses of  $\frac{1}{100}$  to  $\frac{1}{200}$  of a grain. Other forms of medication have been found valueless.

The improvement of the tone of the neurovegetative system through proper measures in vitamin feeding and mild hydrotherapeutic measures in the use of tepid sponge baths seem to be of some value.

3. **Cough.**—Cough is usually the first symptom noticed by the patient, his family or friends, and very frequently is the cause for the examination of the patient and the detection of the disease. This, plus its value in extruding sputum which has collected in the bronchial passages and is causing irritation, are its only two assets.

The mechanism of cough is discussed by Coryllos on page A-154. Cough may cause serious consequences when, in its explosive phase, it may distribute sputum into uninvolved lung tissue. Following the taking of food, in a proportion of individuals with the disease, massage of the bronchial tract results from the passage of food down the esophagus and the loosening of some sputum with consequent bronchial irritation, followed by paroxysmal cough and emesis. In the toxic tuberculous individual such emesis may also follow the aspiration of food because of associated fatigue slowing the function of the epiglottis. In some instances this has resulted in a marked loss of weight and the feeding of such patients immediately after the emesis is recommended and the partaking of food at frequent intervals may sometimes be necessary in the state of extreme fatigue. Fatigue incidental to such conditions as insomnia, or excessive physical exertion, very frequently induces cough and such a cough may be controlled by correcting these habits.

Cough induces cough and the habit should be suppressed where it is not productive of the necessary raising of sputum. Teaching the patient to breathe quietly, suppressing the supposed desire to cough, will frequently do away with its constant sequence.

Nasal pharyngeal infections and paranasal sinus disease, with their dripping of secretions into the lower respiratory tract, may very frequently be productive of considerable coughing in associated pulmonary tuberculous disease. Careful examination for and eradication of these conditions in such instances should be practiced.

The pulmonary cavities, tuberculous or bronchiectatic, if continuous with a patent bronchus and properly drained through posture will also curtail much unnecessary coughing.

The ventilation of the room of the patient, making certain that the humidity is present in adequate relative amounts, may keep the bronchial mucosa in a normal moist condition and avoid the irritation resulting from a drying out of these tissues under certain environmental conditions. The medicinal treatment of cough is directed to:

1. The lessening of sputum.
2. The relaxation of the bronchial passages.
3. Suppression of the irritation in the nerve endings of the bronchial mucosa.

*Home remedies*, such as warm milk, milk and honey, or glycerine or milk and rock candy or other syrups made in the home with brown sugar and onions have, in many instances, been efficacious in giving relief from this symptom. These "*Grandmother's remedies*" may prove of avail and have a psychic element which is of value. To lessen the amount of sputum, creosote may be of value as suggested above.

We also quite commonly utilize small doses of ephedrine, as ephedrine sulphate,  $\frac{1}{2}$  grain to the dose, of a mixture, to lessen secretion and also for its mild antispasmodic action.

As an antispasmodic and also because of its value in lessening secretion, tincture of belladonna may be combined with a simple cough mixture in doses of 5 to 10 minims. Other antispasmodics and sedatives, as hyoscyamus, may be of value. To control the nerve irritation, with the removal of heroin from our therapeutic armamentarium in this country, we depend largely upon codein and, with the exception of the rare case which may manifest an idiosyncrasy to its use, we do not hesitate in giving it to patients in the average dose of  $\frac{1}{4}$  grain at intervals of three to four hours alone or combined with other substances. It has no evident opium toxicity and our experience has not observed any habit-forming characters in its use.

**4. Pulmonary Hemorrhage in Tuberculosis.**—Pulmonary hemorrhage in this disease is a dread symptom to the patient, but the number of individuals with tuberculosis whose lives are terminated by such hemorrhage are limited to approximately 1 to 5 per cent. of the caseous pneumonic group.

The cause of hemorrhage in this disease is given in detail by Jaffé in his discourse on Pathology. A rupture of an aneurism of a pulmonary artery in the walls of the cavity, following coughing or straining, seems to be the most frequent and the most serious cause. It also allows an admixture of blood with caseous material collected in such a cavity to occur, which after it spills over into the adjacent bronchial structure, may cause disease extension.

It is most important in treating this manifestation to put the patient at rest, preferably in a semi-recumbent position, if comfort is attained in that posture. Morphine in  $\frac{1}{8}$  to  $\frac{1}{4}$  grain doses hypodermically should be given where the bleeding is of any consequential amount, or the patient is evidently alarmed. Morphine also tends to abate the cough and prevents the disturbance of any

coagulum which is forming. An ice bag may also be placed on the patient's chest. This latter is largely psychic in its action.

Collapse therapy should be instituted wherever possible in all severe hemorrhages—pneumothorax being the procedure of choice. In instances where adhesions have prevented collapse through gas injection, and recurrent hemorrhages have occurred, it has been necessary to resort to one of the other forms of collapse, dependent upon the pathology present. Phrenicectomy, apicolysis or extrapleural thoracoplasty have had to be recommended under various conditions. It is, of course, necessary to know from which lung the bleeding is occurring, inasmuch as aspiration of blood in the presence of a severe hemorrhage may produce physical findings in the opposite lung.

To increase coagulation of the blood where indications make this necessary, as determined by laboratory tests, it has been my habit within recent years to utilize calcium gluconate intravenously and intramuscularly in 10 grain doses two or three times daily, and at the same time administer viosterol to make certain of the increasing of blood calcium essential in the process of coagulation. The viosterol may be given in pure form intravenously or by mouth in doses of 20 drops three times a day. Other coagulants, such as thromboplastin and coagulose have also been used intramuscularly in amounts of 10 to 20 c.c. at intervals of 12 to 24 hours, as indicated.

Emetin hydrochloride,  $\frac{1}{2}$  grain, intramuscularly, has been used empirically by some individuals where small recurrent hemorrhages have been seen. Its value is questionable as an immediate agent in controlling bleeding, although in our experimentation with this substance, we have found it to cause an avascularity in neoplastic tissue, due to an obliterating endarteritis. The nitrites are recommended and used by many in pulmonary hemorrhage. While their peripheral action is one of vasodilation, they seem to cause an increase in the intrapulmonary vascular pressure. Amyl nitrite may be inhaled from 10-drop glass containers, in which it is dispensed; nitroglycerin in a 1 per cent. alcoholic solution may be utilized in 3- to 4-drop doses in water. In instances where bleeding has been severe, so as to cause a picture of exsanguination, autotransfusion in the bandaging of legs and arms to maintain sufficient blood for the vital organs and centers, may be necessary. Blood transfusion has been resorted to in many instances following such severe hemoptysis.

There are a few patients with pulmonary tuberculosis who also have a hypertension. Such individuals may benefit through venesection to relieve the vascular tension where severe or recurrent hemoptysis may be present. This measure should be employed only with great caution.

The diet should be restricted in the presence of much bleeding and the patient allowed only ice chips in the mouth. As the bleeding is curtailed, cold milk and cream and gelatin preparations may be given in small amounts at frequent intervals to sustain the strength. Where collapse therapy has been employed in the presence of a severe hemorrhage, feeding should continue on almost the normal scale.

In small hemoptysis, while the diet should be somewhat restricted, one should be guided by the condition of the patient and the effect the swallowing movement may have in exciting more bleeding.

As convalescence from hemoptysis occurs, the cough should be controlled through the use of necessary sedatives; concentrated, cool foods should be given in small amounts at frequent intervals, and hemopoiesis should be stimulated through the use of liver extracts, iron, copper, as well as the necessary foods.

5. **Dyspnea.**—Dyspnea may occur in the patient with an extensive pulmonary disease, where a considerable amount of the alveolar structure has been replaced, because of a diminution in gaseous interchange. It may also be found as the result of a severe toxemia in acute exudative lesions of the caseous pneumonic type. In such instances the usual therapeutic régime is most important in aiding through rest to curtail the metabolic needs for oxygen, thereby lessening pulmonary function.

Dyspnea may also be found in temporary bronchial obstruction, resulting in a massive atelectasis. If this be due to a plug of thick mucus, the use of carbon dioxide oxygen inhalations may allow a relaxation of the bronchus so that the plug may be loosened and coughed up. In other instances, removal of the plug may be necessary through a bronchoscope.

The dyspnea in spontaneous pneumothorax may, under some conditions, be relieved by inserting a needle into the pleural cavity, where the type of spontaneous pneumothorax allows such improvement.

In massive pleural effusions the removal of such effusions, not exceeding 1000 c.c. at a sitting unless replaced by air, should prove of value. The dyspnea of an associated asthma should receive treatment for that condition. The use of antispasmodics, such as adrenalin and ephedrine, are indicated. Where much discomfort is present in patients with this associated manifestation, almost instantaneous relief may be received through the use of the following combination hypodermically:

R Morphine sulphate . . . . .	1/6 grain
Atropin sulphate . . . . .	1/150 grain
Nitroglycerin . . . . .	1/100 grain
Adrenalin 1 1000 . . . . .	10 minims

One should also not overlook the temporary psychic dyspnea associated with fright or worry. The confidence, instilled after a short conversation with the patient, may cause this latter to disappear.

6 **Insomnia.**—Many patients complain of an inability to sleep when placed on absolute general rest, or insomnia may develop at any time in the course of treatment. Careful attention to the surroundings of the patient and the establishment of a zone of quiet may be of aid. Arrangement of the bed and bedding is most important. In warm weather too much clothing, or in cold weather too little clothing, may allow discomfort to cause a sleepless night. Adequate protection of the patient on his porch or in his room from storms which occur at night should also be provided to prevent the loss of sleep.

In many cases a sense of alarm may occupy the mind of the patient. The presence of a nurse or calm attendant at the bedside may do much to remove fears, which oftentimes are only temporary, and thus allow somnolence.

Progressive relaxation, as advocated by Jacobson and briefly discussed in the chapter on Rest, is a most important adjunct.

A glass of warm milk on retiring may be of value. A mild, superficial massage may soothe or calm some individuals. *Hypnotics*, where necessary, should be resorted to. An abundance of various types of such drugs are on the market. I do not recommend their promiscuous use. Such substances as allonal, veronal, sodium amytal, sedormid, prepared by various proprietary drug houses, may be given in the average doses recommended for their use.

**7. Chest Pains.**—Chest pains associated with pulmonary disease may be due to pleurisy, intercostal neuralgias, myalgias, or may be referred from associated *intrathoracic or abdominal conditions*. One should also not overlook the rare association of a tuberculous spondylitis, producing pains radiating along the intercostal nerves in the zone of disease involvement. Counterirritants may be utilized to relieve the pain of pleurisy or inflammations in the muscle or nerve root. Moist heat is most beneficial and soothing applied as a fomentation. A thin application of tincture of iodine in those individuals who have not sensitive skins may also be of benefit. Mustard plasters are also at times found to be efficacious.

The increase in extension of our knowledge in creating deep-seated heat, through the use of diathermy, has given a method which will bring relief when other counterirritants may fail.

Analgesics, in the form of the coal-tar products, combined with codein where necessary, and only in rare instances a small dose of morphine, can be resorted to.

**8. Cardiovascular Manifestations.**—The chapter on this condition goes into great detail as to the various abnormal conditions found affecting this system. Their treatment is largely a matter of detailed supervision of the usual régime, particularly as to rest.

The patient having a tachycardia which is present on bed rest, or appears on the slightest exertion or psychic reaction, should be maintained on general rest until these manifestations have disappeared. Distortion of the large tributaries of the heart occurring with mediastinal displacement due to extensive fibrosis may at times produce palpitation and a feeling of cardiac distress, which may not be relieved by rest. In such instances, where the type and extent of pathology permit, thoracoplastic surgery has been recommended and has proved of avail. With extensive bilateral pathology this course is impossible and sedatives have to be resorted to.

Gastrointestinal disturbances may cause abdominal distention with cardiac embarrassment, necessitating careful dietary supervision to prevent recurrences of this condition.

In progressive cases with a marked toxemia and debilitation, the heart muscle gradually suffers and eventually manifests a lack of tone which is evidenced by its inability to cope with the normal demands of circulation. Dyspnea, cyanosis,

passive congestion of the bases of the lungs, the liver, and edema of the ankles may be seen. The picture of decompensation of the right heart is also found in those instances where extensive fibrosis of the pulmonary tissue creates a stenosis of the pulmonary vessels, particularly the arteries, impeding the circulation of blood and causing a back pressure with right heart failure.

*Digitalis therapy* should be utilized in such cases and may afford temporary relief. Strychnine, camphor in oil and caffeine sodium benzoate may also prove of value, especially where the tendency is for acute heart failure. Whisky, orally or rectally, or hot, strong coffee per rectum may be of value in the acute collapse. The severe discomfort associated with marked dyspnea or air hunger may only be relieved by opiates.

The skin, particularly that of the lower extremities, should be carefully protected where edema is present and small gauze rings utilized to prevent rubbing against the linens with attendant discomfort.

9. **Gastrointestinal Disturbances.**—(a) *Anorexia*.—Patients with a toxemia tend to develop a loss of appetite. Under the proper régime this, however, tends to disappear, especially where adequate room ventilation and rest are had. In other instances one may find patients who have attempted forced feeding and have ingested unusually large amounts of food, which has created gastrointestinal disturbances and a marked anorexia, which may persist for some time. Idiosyncrasies to certain foods may cause anorexia to develop, or food prepared unappetizingly may become repugnant. The tendency on the part of some cooks to prepare the same menu on the same day creates a monotony which may oft-times result in anorexia.

The surroundings of the patient may likewise create psychic difficulties and disgust, affecting the appetite. The correction of these conditions is self-evident. The patient and his attendants should be given information pertaining to the correction of any of the above conditions that are found present. The importance of food and the taking of those foods which are absolutely indicated should be stressed. At times we have found the addition of some vitamin B, in the form of brewers' yeast tablets, of value in stimulating appetites. Other stomachics, such as tincture of gentian in 30 minim doses, have only been used at very infrequent intervals.

(b) *Dyspepsia*.—Dyspepsia may be the result of changes in the gastric secretory mechanism, in which hypochlorhydria or hyperchlorhydria may be found. In many instances the decrease in the acid content of the gastric juices calls for an addition of dilute hydrochloric acid, which may be given the patient in amounts of 5 to 10 minims in a glass of warm water, to be sipped through a glass tube beyond the teeth, at mealtime. Tincture of nux vomica may also improve the gastric secretion. One should not overlook those instances where a primary anemina may be an associated factor.

Where an excess amount of hydrochloric acid is found in the gastric secretion, one should determine if organic pathology in the form of a gastric or duodenal ulcer is present. Where a simple hyperchlorhydria is evident, placing the patient on a demulcent diet and dividing the food into six small meals instead of three

large ones may satisfy the digestive needs. In other instances belladonna as the tincture in 10 minim doses, or the extract in doses of  $\frac{1}{6}$  to  $\frac{1}{10}$  of a grain, combined with magnesium oxide, 5 grains, when slight additional laxative action is needed, or calcium carbonate, 5 grains, to lessen the number of stools, given with bismuth subcarbonate, 15 grains, may be used before meals.

Dyspepsia, as stated above, may be associated with overfeeding. Fever is sometimes found in patients having dyspeptic manifestations, especially those resulting from overfeeding.

(c) *Constipation*.—This is a common symptom and in many institutions the term "cathartic rounds" signifies the afternoon visit of the physician at which time he is plied with requests from patients for such medication.

Wherever possible the diet should be adjusted to provide an adequate amount of roughage to stimulate the peristalsis which has become dormant on bed rest. The use of adequate amounts of fruits, preferably stewed, may tend to overcome this symptom.

One must also not overlook constipation that may be produced by various drugs in the treatment of other complicating conditions present. Some patients may have an idiosyncrasy to certain foodstuffs which stimulate a laxative action, as buttermilk and tomato juice, and these may make unnecessary the feeding of laxatives.

When catharsis must be used, the milder forms should be utilized, giving preference to milk of magnesia, phenolphthalein and mineral oil. Severe catharsis should only be applied with caution. The more severe forms of intestinal derangement associated with enterocolitis are treated in a special chapter.

### TUBERCULIN THERAPY.

Tuberculin, given to the world as a specific for the cure of tuberculosis by Robert Koch in 1890, fell into almost immediate disrepute because of the high fatality percentage following its use. The large doses (1 mg.) given initially and repeated at intervals until reactions were no longer evident and then increased, or until death ensued, are sufficient explanation for the fears and terrors created from its use. Temerity having developed, a small group of phthisiotherapists again began its cautious use. This group included most prominently such men as Goetsch, Trudeau, von Ruck, and Petruschky. The number and type of tuberculins which have been developed are almost synonymous with the number of workers in this special field. Only a few of these preparations have survived. Those used therapeutically at this time are practically limited to the following:

*Tuberculin, "Old" (O. T.)* or Koch's original Tuberculin, is prepared from glycerin bouillon cultures. The concentrate, resulting from the evaporation of the culture to  $\frac{1}{10}$  its original bulk, is sterilized and filtered. The product is, therefore, essentially a glycerin bouillon extract of tubercle bacilli.

*Tuberculin Residue (T. R.)*. Living dried tubercle bacilli are thoroughly ground in a ball mill and extracted in water. The extract is diluted with

glycerin and standardized to contain the residue of 10 mgs. dried bacilli per c.c.

*Bacillen Emulsion (B. E.).* Dried pulverized bacilli are suspended in water and glycerin. After some days the supernatant fluid is separated from the sediment and is standardized to represent 5 mgs. tubercle bacilli per c.c.

*Broth Filtrate (B. F.) Denys.* The unheated, unconcentrated, porcelain filtered bouillon culture of human tubercle bacilli.

**Indications for Tuberculin Therapy.**—Numerous hypotheses have been advanced to explain the indications upon which tuberculin therapy is based and experimental evidence has been presented to corroborate such statements. None of the data, however, can be applied to clinical tuberculosis without certain reservations.

The only condition where tuberculin in the restricted therapeutic dosage may seem to be of value is in the localized, limited, quiescent apical tuberculous lesion. Here, inasmuch as natural forces have built up a wall of fibrotic resistance, its value is doubtful, as such lesions are in the process of healing. Tuberculin is also used in some forms of extrapulmonary tuberculosis, ocular, genitourinary, glandular and skin tuberculosis being the forms favored by some therapists in these special fields.

During recent years it has been generally agreed that any beneficial result that may occur from tuberculin injection is due to the mild inflammation which is produced at the focus of the tuberculous disease. The reactivity of the tissue cells about the tuberculous lesion in the presence of infinitesimally small doses of tuberculin, it is hoped should only elicit a very slight response, increasing the vascularity in the region and irritating the fixed tissue cells to greater fibrous tissue formation without the production of a marked increase in the capillary permeability and its dangerous outpouring of exudate.

**Contraindications.**—Some two decades ago I personally was the recipient of several courses of tuberculin therapy and gave tuberculin therapeutically for a period of over three years. The observations gleaned in the careful supervision of patients with pulmonary tuberculosis who were under detailed control in institutions did not yield results that improved upon the ordinary therapeutic regimen. There were, however, in many instances focal reactions which apparently increased the extent of tuberculous lesions. To those who would still attempt to use this substance in the treatment of pulmonary tuberculosis, we would say that the febrile case is a definite contraindication. Even given in the infinitesimally small doses, untoward reactions may be seen, evidenced as the focal reaction at the site of injection. The focal reaction in the area of disease, which as mentioned is associated with an increased capillary permeability and vascularity in the disease area, allowing an outpouring of exudate, resulting in greater toxin absorption, creates the constitutional reaction. The latter is the result of such toxemia and is manifested by headache, backache, fever, increased pulse rate, etc. On two separate occasions have I seen a late generalization (acute miliary tuberculosis) develop in adults consequent upon such reaction,



in patients who apparently were progressing favorably under the graduated dosage of tuberculin. Cases under observation have also in several instances been found to develop an hemoptysis in the course of a focal reaction. The benefits have been so questionable and largely psychic in their nature and the dangers relatively great, even under most careful usage of this substance, that for many years we have avoided its therapeutic proclivities. We would rather insist that the practitioner utilize the other usual forms of therapy in the management of this disease.

*Technic of Treatment.*—Inasmuch as very minute doses of tuberculin are used, a special syringe has been devised which is carefully calibrated for such small dosage. In extrapulmonary tuberculosis, where tuberculin is used, or for those who, despite warning, attempt to apply it in the pulmonary disease, we would suggest a maximum dosage at the start of 0.000,000,1 gram ( $\frac{1}{1000}$  of a mg.). Those individuals showing any marked evidence of an exudative process should be given a smaller initial dosage—0.000,000,01 to 0.000,000,001 gram—( $\frac{1}{10,000}$  of a mg. to  $\frac{1}{1,000,000}$  of a mg.), the idea being to keep within a point of reaction and thus attempt to raise the tolerance of the individual to tuberculin to a higher level, increasing the dosage correspondingly to the new level. Ornstein and Ulmar, in attempting to create a beneficial result in their severe exudative lesions of the caseous pneumonic type, evidencing recurrent acute allergic manifestations, have used tuberculin in the hope of desensitizing these individuals and lessening their reactivity, utilizing the bacillen emulsion. The injection may be given in the intrascapular region or at the margin of the deltoid muscle. It is best given in the late afternoon and the patient should be kept in bed during the period of forty-eight hours following its injection, a careful record of temperature, pulse and other subjective symptoms being kept to denote any reaction. The temperature during the day should be taken at intervals of two hours. The injections should be given at intervals of three days and increased according to the table below.

In the event of a focal reaction, treatment should be temporarily stopped until evidences of the toxemia produced by the reaction have disappeared and the dosage should be stepped back to a point two or three injections previously within the point of reactivity of the patient. The dilutions are prepared by taking eight brown bottles (to protect the contents from sunlight), having them properly sterilized, covered with a rubber diaphragm stopper, placing within each of them 9 c.c. of normal salt solution with 0.25 c.c. of phenol. The container of pure tuberculin constitutes bottle No. 1. From this 1 c.c. is taken and placed in one of the brown bottles, which becomes solution No. 2 and contains 100 mg. per c.c. of tuberculin. One c.c. of solution No. 2 is placed in another bottle with its diluent, making solution No. 3, containing 10 mgs. per c.c., and so on down through to solution No. 9, which contains  $\frac{1}{100,000}$  of a mg. per c.c. The table below gives the dilution and progressive dosage we have used in such therapy:

Injection should be given every Tuesday and Friday. Begin Treatment once Each Week.

Solution No. 9 (1/100,000 mg. per c.c.)		Solution No. 8 (1/10,000 mg. per c.c.)		Solution No. 7 (1/1000 mg. per c.c.)	
Dose 1	0.1 c.c.	Dose 7.	0.1 c.c.	Dose 13.....	0.1 c.c.
Dose 2	0.2 c.c.	Dose 8	0.2 c.c.	Dose 14.....	0.2 c.c.
Dose 3	0.3 c.c.	Dose 9	0.3 c.c.	Dose 15 .....	0.3 c.c.
Dose 4	0.5 c.c.	Dose 10	0.5 c.c.	Dose 16.....	0.5 c.c.
Dose 5	0.7 c.c.	Dose 11	0.7 c.c.	Dose 17.....	0.7 c.c.
Dose 6	0.9 c.c.	Dose 12	0.9 c.c.	Dose 18....	0.9 c.c.
Solution No. 6 (1/100 mg. per c.c.)		Solution No. 5 (1/10 mg. per c.c.)		Solution No. 4 (1 mg. per c.c.)	
Dose 19	0.1 c.c.	Dose 23	0.1 c.c.	Dose 37....	0.1 c.c.
Dose 20	0.2 c.c.	Dose 29	0.2 c.c.	Dose 38.....	0.2 c.c.
Dose 21	0.3 c.c.	Dose 30	0.3 c.c.	Dose 39.....	0.3 c.c.
Dose 22	0.4 c.c.	Dose 31	0.4 c.c.	Dose 40....	0.4 c.c.
Dose 23	0.5 c.c.	Dose 32	0.5 c.c.	Dose 41....	0.5 c.c.
Dose 24	0.6 c.c.	Dose 33	0.6 c.c.	Dose 42..	0.6 c.c.
Dose 25	0.7 c.c.	Dose 34	0.7 c.c.	Dose 43..	0.7 c.c.
Dose 26	0.8 c.c.	Dose 35	0.8 c.c.	Dose 44..	0.8 c.c.
Dose 27	0.9 c.c.	Dose 36	0.9 c.c.	Dose 45.....	0.9 c.c.
Solution No. 3 (10 mg. per c.c.)		Solution No. 2 (100 mg. per c.c.)			
Dose 46	0.1 c.c.	Dose 55	0.1 c.c.		
Dose 47	0.2 c.c.	Dose 56	0.2 c.c.		
Dose 48	0.3 c.c.	Dose 57	0.3 c.c.		
Dose 49	0.4 c.c.	Dose 58	0.4 c.c.		
Dose 50	0.5 c.c.	Dose 59	0.5 c.c.		
Dose 51	0.6 c.c.	Dose 60	0.6 c.c.		
Dose 52	0.7 c.c.	Dose 61	0.7 c.c.		
Dose 53	0.8 c.c.	Dose 62	0.8 c.c.		
Dose 54	0.9 c.c.	Dose 63	0.9 c.c.		

The dilutions should be made fresh every month.

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## SECTION D.

(Chapters XIX to XXIV.)

### COLLAPSE THERAPY.

Artificial Pneumothorax, Intrapleural Pneumolysis, Oleothorax, Phrenic Neurectomy, Surgical Selective Apical Collapse, Extra-Pleural Thoracoplasty.

## CHAPTER XIX.

# ARTIFICIAL PNEUMOTHORAX.\*

RALPH C. MATSON.

### INTRODUCTION.

It is a common observation that the majority of cases of pulmonary tuberculosis, in the early and many in the moderately advanced stages, recover as a result of the usual sanatorium regime, provided they can be persuaded and are in a position economically to continue the program sufficiently long. The benefit of this course of treatment, whether it be carried out in an institution or at home, may be ascribed principally to rest. However, it is generally agreed by those who have had a long experience in the treatment of pulmonary tuberculosis that where the disease has advanced to a more extensive infiltration with cavity formation, healing may take place following prolonged bed rest, but in the majority of cases it sooner or later progressively invades the opposite lung, larynx or gastrointestinal tract and becomes irremediable. There is almost a unanimity of opinion then that something more is indicated than routine rest and hygienic, dietetic, physical therapy in the greater number of cases where a tuberculous infiltration of more than *minimum* extent, with a positive sputum, is present.

The common default of bed rest to fulfill the desired end-results in a large proportion of even moderately advanced cases, especially those with cavity formation, has incited the development of other methods of treatment. The failure to find a curative sera or chemotherapeutic substance which alone very much influences the course of the disease and the fact that functional rest of the lung is the most important detail of routine sanatorium care, has naturally been a direct stimulus to develop means for providing additional rest for the lung and to bring the walls of cavities together so that healing may take place. It was obvious to those recognizing the failure of sanatorium care in so many cases that a method giving greatest hope of accomplishing what was wanted,—namely, more functional rest than that provided by bed and postural rest alone, as well as providing means of closing cavities, was to be found in surgical or at least operative procedures. As a consequence, numerous operations have been advocated from time to time, but many have passed into obscurity; practically the only ones having certified their merit are those included under the term "operative collapse therapy," and have as their objective functional rest of the lung and closure of cavities obtained in the mechanical way through collapse of the lung.

Now that sufficient time has elapsed to uphold a conclusion as to the value of collapse therapy, one may safely say that it is the only real contribution to

\* This contribution is based upon studies and material from the combined services of myself and associates, Dr. Ray W. Matson and Dr. Marr Bisailon.

the treatment of pulmonary tuberculosis in the past half century. Of the various operative collapse methods, artificial pneumothorax has proved the most valuable and will therefore be considered first.

### HISTORICAL.

To James Carson, a Liverpool physician, is generally given the credit of having first proposed artificial pneumothorax more than a century ago. However, Allen K. Krause<sup>1</sup> calls attention to a statement in Thomas Young's book on "Consumptive Diseases" published in 1815, wherein he refers to a method of treating adhesive pleuritis, attributed to the Hippocratic school, which, in every essential, is that of artificial pneumothorax. Krause quotes from the second book "On Affections," found in Littré's bilingual text of Hippocrates, referring to the treatment of "the lung inclining against the side," the statement, "if this affection results from a wound or as sometimes happens from an incision for empyema, one should attach a pipe to a bladder, fill the bladder with air and send it into the interior of the chest," claiming by this method the very best results will be obtained. By the expression, "the lung inclining against the side," Littré believes Hippocrates means empyema. Krause states, "at any rate, the therapeutic method described is plainly that of inflating the chest with air, and we must believe it was actively practised more than 2000 years ago . . . . Young's comment leaves no doubt that more than 100 years ago, he, for one, partially grasped the underlying principle of the procedure."

Seven years after Young's treatise appeared, or in 1822, Carson<sup>2</sup> urged a trial of artificial pneumothorax, in a series of physiological essays. In these he wrote most authoritatively of the value and possibility of artificial pneumothorax in the treatment of phthisis and other diseases, based upon animal experiments. Carson had it attempted on two patients, but his recommendations were never further applied at that time for therapeutic purposes.

In 1837 William Stokes<sup>3</sup> directed attention to the marked improvement in a case of phthisis following spontaneous pneumothorax.

Toussaint,<sup>4</sup> in 1880, advocated collapse of the lung, and two years later, Carlo Forlanini<sup>5</sup> of Pavia proposed it, but did not put it to practical test until 1888, reporting his experiences in 1894.<sup>6</sup> Several years later, John B. Murphy<sup>7</sup> urged utilization of the method and reported five cases. Despite the approbation of this new therapeutic method, it was given trivial regard until Brauer<sup>8</sup> published the results of his work in 1905 and 1906. We are indebted to Brauer for many contributions of great scientific value which directed worldwide attention to this mode of treatment. His work activated interest throughout Europe and America, and artificial pneumothorax gradually made a definite place for itself in tuberculosis therapy. Today, phthisiotherapeutists everywhere recognize it as a method indicated in certain types of pulmonary tuberculosis.

### MODE OF ACTION.

An explanation of the favorable action of artificial pneumothorax upon a tuberculous lung does not seem difficult. The collapsed or compressed lung is no longer an air-containing organ in constant motion but becomes essentially an immovable body of solid consistence, and the tuberculous process, instead of

its characteristic tendency to form cavities in the lung, now conducts itself similarly to that of solid tissue with a tendency to fibrous tissue production. So that healing may take place, the walls of cavities are pressed together and held at rest. The result of the pure mechanical action, or compression, upon the destructive process is that the tuberculous sputum and caseous débris are pressed out of the air-containing soft parts opening into a bronchus, like water squeezed from a sponge. The extension of disease, through aspiration of sputum or blood in the healthy parts of the lung, is made more difficult through fixation of the lung and compression of the finer bronchi and alveoli. All small lymph and blood-vessels are compressed and the resorption of toxins from the diseased area is more or less prevented. Clinical proof of this is the fall of temperature which frequently takes place after the first few introductions of gas. Corresponding to the compression of the capillaries, the blood circulation becomes slower, especially in the arterial portion of the lung circulation, whose carbonic acid content in the blood is accordingly distinctly increased. This venous congestion, in combination with the lymph stasis, causes, perhaps, the profuse scar tissue formation, and it would not be impossible that it also exerts a local auto-tuberculinization by inhibiting the growth of tubercle bacilli. The experiments of Bruns,<sup>9</sup> Begtrup-Hansen<sup>10</sup> have proved that the curative value is not due to Biers' hyperemia theory as was formerly thought, for the blood content of the compressed lung, in spite of arterial congestion, is distinctly less than in the other lung. Clinical observation confirms this, for, after shutting off the function of the one lung, the blood must pass through the other for oxygen absorption, and if its blood content were not higher than normal, a respiratory insufficiency would exist. However, we observe no increase in respiration while the patient is at rest. After the organs have become accustomed to new pressure conditions, the oxygen absorption from the noncompressed lung takes place as normal and its blood content is accordingly greater. The hyperemia explains the favorable influence compression of the badly diseased lung produces on a not too far advanced disease on the opposite side, which is further benefited, as is the whole body, by the cutting off of toxin production and resorption on the compressed side. At the same time, it must be pointed out that in cases with extreme disease on one side and active disease on the other, the patient's condition may be aggravated by the increased function and consequent toxin liberation following collapse.

**Indications.**—The indications for an artificial pneumothorax vary within the widest limits, and every individual case represents a problem for the physician to solve on a basis of his experience in the usual treatment and in pneumothorax therapy. Early infiltration cases with a negative sputum may be withheld, for they usually recover without collapse therapy. However, after three months' observation in a given case (if an early one), a careful study of the clinical record, and comparison of the physical examinations and roentgen films should help strengthen a decision as to whether collapse therapy should be utilized.

In cases of pulmonary tuberculosis with beginning infiltration and positive sputum, as well as moderately advanced cases, if, after a reasonable trial of strict sanatorium treatment (three or four months), the disease is progressive or not

responding satisfactorily to treatment, artificial pneumothorax should be instituted. The treatment should be used before destructive lesions are established and adhesions prevent a satisfactory collapse of the lung. Hemoptysis, whether slight or severe, is an obligatory indication for artificial pneumothorax, providing it is possible to determine in which lung the bleeding is taking place. Tuberculous

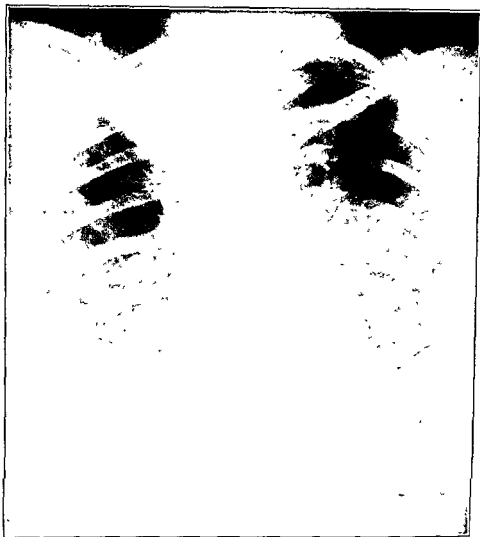


Fig. 1—Caseouspneumonic tuberculosis with stationary cavity right and progressive metastatic extension in the left lung. Sputum 50 c.c. Tubercle bacilli positive. Artificial pneumothorax impossible on the right side because of pleuritic adhesions.

spontaneous pneumothorax should be converted into a controllable artificial pneumothorax. Tuberculous pleurisy with effusion should be treated by replacing the fluid with air and an artificial pneumothorax maintained according to the indications of the underlying disease.

The most favorable results will be achieved in caseouspneumonic types of tuberculosis with essential freedom from disease in the contralateral lung. In



progressive fibrocaseous cavernous types of disease, with lesions more destructive in character, the end-results are somewhat less satisfactory. However, in active, advancing caseouspneumonic and bronchopneumonic types of tuberculosis, in spite of statements to the contrary, one sees splendid results, providing a satisfactory collapse of the lung can be established. In unilateral cavity cases, the

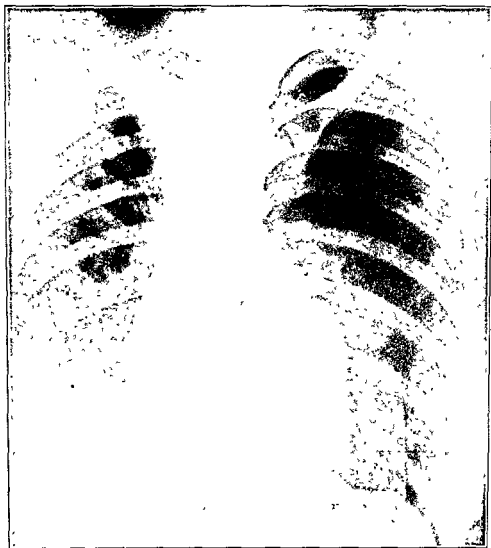


Fig 2.—Same case as Fig. 1; six months later. Sputum 5 c.c. Tubercle bacilli negative.

sooner a pneumothorax is established, the better it will be, for not only is the danger of extrapulmonary metastatic infection diminished, but the possibility of an extension to the same lung or contralateral lung is lessened.

While it is desirable to have the disease confined to one side, the presence of even an active disease in the contralateral lung does not contraindicate pneumothorax treatment, provided it is not too extensive or of an acute infiltrating or rapidly advancing character. In cases with a more or less stationary, well

fibrosed cavity on one side, and an otherwise good lung, with an active, advancing metastatic spread to the contralateral lung, artificial pneumothorax should be instituted on the contralateral side. If the mediastinum is labile one is often able to obtain sufficient displacement of it to effect closure of the cavity at the same time. This practice is contrary to the generally accepted procedure,—namely, to collapse the cavity side first, then establish a pneumothorax on the contralateral side, if necessary, and continue the case as a bilateral pneumothorax.

Our interest in this procedure was the result of an observation several years ago upon a young female with a stationary cavity in the right upper lobe and a metastatic spread to the contralateral lung. Several months previously, she had had an acute exudate formation upon the right side, which was treated by aspiration without air replacement. At that time, the contralateral lung was essentially free of any extension. Gradually, however, the extension of disease to the opposite lung took place; upon her entrance into our service, she presented a circumscribed stationary cavity in the upper lobe of the right lung, extending from the apex to the second rib anterior. The lung was otherwise essentially free of disease; the pleura was thickened and the phrenicocostal angle obliterated. Retractive changes indicated unquestionable obliteration of the pleural cavity by adhesions. In the left lung was a metastatic spread, which, after three months' observation, advanced in spite of strict sanatorium care. An artificial pneumothorax was established upon the left side, which presented the fresh extension, and as the lung was collapsed, the cavity on the other side became smaller. Finally, when compression replaced collapse, the mediastinum shifted to the right and the cavity closed. The patient's cough and expectoration disappeared and her sputum became negative (Figs. 1 and 2). We have repeatedly utilized this procedure with success in other cases of this type.

*Bilateral pneumothorax* is indicated in cases where a pneumothorax has been established on one side and the contralateral lung is suddenly invaded with an acute metastatic caseous pneumonia or bronchopneumonia (Figs. 3, 4, 5,) or when the contralateral lung shows signs of progressive disease; it is also indicated in bilateral cavity cases. The degree of collapse each side should have depends upon the underlying pathology. If one lung is completely collapsed, bilateral pneumothorax should not be attempted unless an emergency arises, such as hemoptysis from the contralateral lung. If time permits, it is safer to let the first collapsed lung expand sufficiently to maintain life, in case a spontaneous pneumothorax should occur on the second side.

Both sides must never be started simultaneously. In far advanced, bilateral or so-called "hopeless" cases, both lungs being extensively involved, one might be tempted to institute a pneumothorax first on one side and then on the other—for humanitarian reasons. When the disease is of a progressive character, with manifest intestinal lesions, the benefits are slight, impermanent, and do not justify the procedure. Contrariwise, bilateral pneumothorax is upheld even in extensive bilateral cases of a slowly progressive type—if the patient is in good condition without intestinal or painful laryngeal involvement.

**Contraindications.**—Cardiorenal disease, or extensive emphysema, is an absolute contraindication for pneumothorax. Tuberculosis of the larynx and intestines is no contraindication, unless interfering with nutrition and of a progressive character. Controlled diabetes is no contraindication. Asthma, if its cause can be determined and the paroxysms controlled, is no contraindication,

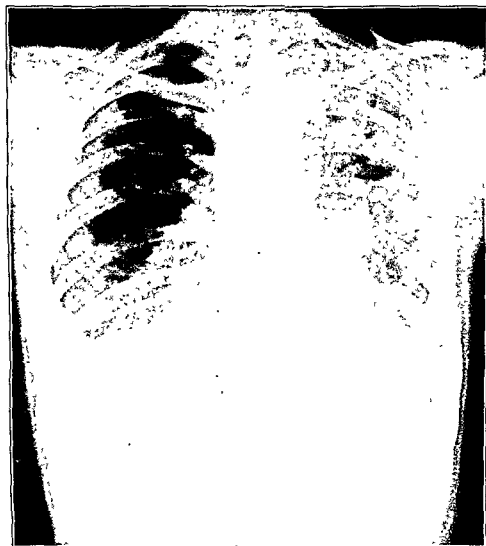


Fig. 3.—Caseous-pneumonic tuberculosis with cavity in the left lung—several metastatic extensions in right lung. Temperature 101°-102° F.; weight 102 pounds. Sputum 20 c.c., tubercle bacilli positive. Pneumothorax begun left side.

but when the paroxysms cannot be controlled, it is an absolute contraindication. Renal tuberculosis is no contraindication. We have had no experience with children under twelve. However, age *per se* should not be considered a contraindication. Pregnancy is, in our experience, no contraindication.

**Selection of Cases.**—Artificial pneumothorax is not intended to replace the routine physical, hygienic, dietetic régime which constitutes the basis of modern

sanatorium care of pulmonary tuberculosis. It is not designed to supplant other recognized methods of treatment. Not all physicians are in a position to employ it, as, by incorrect application, injury can come about. One must not only understand artificial pneumothorax treatment (which varies with the individual) but one must have a knowledge of tuberculosis from a pathological, clinical and roentgenological standpoint.



Fig. 4.—Same case as Fig. 3. Two months later—caseous-pneumonic tuberculosis in right lung. Temperature 102°-103° F. Sputum 25 c.c. T.B. positive. Weight 99 pounds. Pneumothorax begun on right side and bilateral pneumothorax continued.

In the selection of cases the roentgen-ray plays a very important rôle, enabling one not only to select suitable cases by establishing the indications and contraindications, but provides a means to graphically follow the anatomical distribution of the lesions, their character, the degree of collapse or compression, and the presence and distribution of adhesions, and thus safeguard the other side.

In cases with extensive destructive changes on the one side, producing marked auscultatory phenomena, it is exceedingly difficult to pass judgment upon the integrity of the contralateral lung, especially posterior, where râles are often transmitted to the opposite side with such intensity that refined tones on the contralateral side cannot be heard. Even in 1856, Feuger directed attention to the echo of bronchial breathing from the diseased to the opposite healthy lung. Since

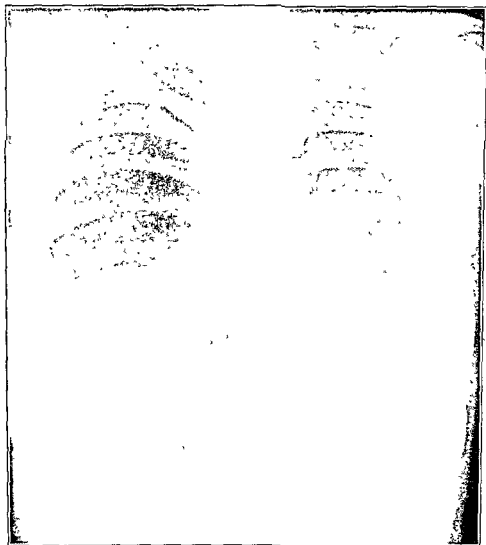


Fig 5.—Same case as Figs. 3 and 4, one and one-half years later. Left lung nearly expanded. Right lung satisfactorily collapsed in spite of adhesions. Temperature normal. No sputum. Weight 124 pounds.

then, Budde and others have called attention to the conduction phenomenon of râles. At times, one is astounded at the amount of disease shown upon the roentgen film which has escaped a most thorough physical examination. Cases which have been considered essentially unilateral, as a result of physical examination, will often disclose extensive disease in the supposedly good lung, as the

result of roentgenological examination, especially when a metastatic infection of the central portion of the lung has taken place. The roentgen-ray reveals the character and extent of this type of disease with a certainty not otherwise obtainable. Furthermore, in cases with severe, acute infiltrating disease upon one side and compensatory changes upon the other, the respiratory sounds are so altered that it is difficult to determine the extent of disease by physical examination.

From a roentgenological standpoint, circumscribed hilus tuberculosis characterized by round and oval uniform areas of increased density; hilus-apex tuberculosis with isolated areas in the apex; increased peribronchial and perivascular paths; also somewhat more extensive disease with scattered areas in the apex and upper lobe, but isolated in the lower lobe, do not contraindicate collapse of the opposite side. However, if one finds confluent areas of consolidation, bronchopneumonic or rapidly advancing destructive processes in the upper lobe, collapse of one lung is contraindicated; bilateral pneumothorax may then be considered. Needless to say, the roentgenological findings must be interpreted with utmost foresight and only by one thoroughly familiar with the pathology of tuberculosis. The phthisiotherapist himself must make the interpretation, exercising much caution in diagnosing small cavities on the single film alone, as bands of adhesions, circularly arranged, not infrequently resemble cavities.

*Surgical Intervention in the Presence of an Artificial Pneumothorax.*—We have repeatedly subjected patients with complete pneumothorax to surgical procedures necessitating a general anesthesia. Aside from the frequent occurrence of exudate in the pneumothorax cavity, following pregnancy or abortion, we have observed no ill effects from operation, which should be performed under gas anesthesia and ought not to be prolonged.

*The Value of Pneumothorax on the Right and Left Lung.*—According to our experience, the left lung has required artificial pneumothorax more often than the right lung, and the results have been more successful. This relative degree of success is probably attributable to the fact that a pneumothorax is not so well tolerated on the right side because of the effects of pressure upon the right heart and superior vena cava.

*Technic.*—We believe that patients subjected to pneumothorax therapy should have the first induction in an institution. Even then it is not well to begin a pneumothorax if, after spending a short time in an institution, the patient's resources are exhausted and he will be forced to resume work. In other words, a pneumothorax should not be started unless one can have valid surety that it can be brought to a satisfactory conclusion. Conceding that indications are very obvious from a clinical standpoint, the patient must be apprised of the purpose of artificial pneumothorax and a searching inquiry made to learn if he is in a position, economically and socially, to cooperate. Consideration of the patient's finances is urgent, as patients whose financial resources make it necessary for them to enter a public institution (if admittance will be reasonably prompt and no emergency exists) might better defer pneumothorax treatment until it can be instituted and continued by the same physician. The technic of establishing a pneumothorax is fairly well standardized, but must be individualized in each case. Consequently, the subject will be dealt with in a general way.

**Apparatus.**—Scarcely a month passes by that some new pneumothorax apparatus is not described in medical literature. Each author claims some unproven ascendancy of his instrument, and as time goes on, instead of advancing in simplicity, they are becoming more expensive and more complicated to the beginner. Elaborate, intricate technical apparatus will not compensate for inexperience; so whether the operator has had a pneumothorax practice or not,

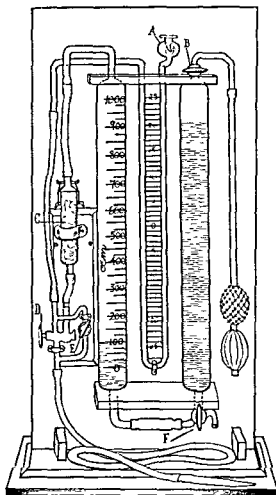


Fig. 6—Forlanini-Saugmann's Pneumothorax Apparatus. *A*, manometer. *B*, stopcock regulating flow of gas. *C*, filter. *D*, stopcock controlling the manometer and the outflow of gas. *E*, stopcock controlling manometer. *F*, stopcock controlling opening for filling or draining the apparatus.

apparatus and instruments of quite simple design suffice. The Forlanini-Saugman, Gassis, Robinson, and Singer are reputable equipments and can be relied upon. An apparatus which provides the possibility of either introducing gas or removing it is preferable. We have employed the Forlanini-Saugman\* (Fig. 6) and the Gassis † (Fig. 7) for years; of the two, the latter is preferable,

\*Manufactured by Hauff and Brust, Berlin, N.W., Luiesenstrasse, 67.

†Manufactured by Kny Shearer, Corp., 580 Fifth Ave., New York, N. Y.

as one may, with equal ease, introduce gas or remove it. A typical pneumothorax apparatus comprises a reservoir of gas and one for water, or some solution to replace the gas as it is introduced into the pleural cavity. A water manometer is an obligatory part of the outfit, as it, first of all, safeguards against gas embolism by revealing information as to whether the needle is in free pleural

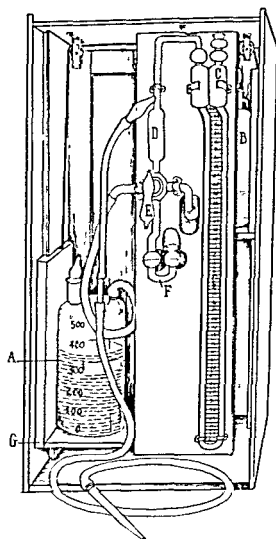


Fig. 7.—Gassis portable pneumothorax apparatus. *A-B*, bottles resting on platform (*G*) elevated or lowered for introducing or aspirating gas. *C*, manometer. *D*, gauze filter. *E*, control stopcock. *F*, air intake or outlet filled with anti-septic solution.

space or otherwise; secondly, it enables one to measure the intrapleural pressure. The gas and water reservoirs should have a 500 to 1000 c.c. capacity. The manometer should be of sufficient length to provide readings of at least 25 cm. positive or negative water pressure.

*Pneumothorax Needles.*—A large variety of pneumothorax needles have been designed for introducing gas into the pleural cavity, with a view of performing



the operation in the safest possible manner. Two kinds of needles are preferred by those most experienced in pneumothorax therapy—one for primary inflations and the other for refills. For the primary inflation, it is essential to have a needle sharp enough to be capable of penetrating the chest wall and blunt enough to avoid danger of puncturing the lung. These requirements are found in the trocar and cannula type of needle. For the past twenty years, after trying numerous types of needles for insufflation, we cling to the Solomon blunt needle and cannula, as modified in our clinic, for primary injection of gas (Fig 8) For

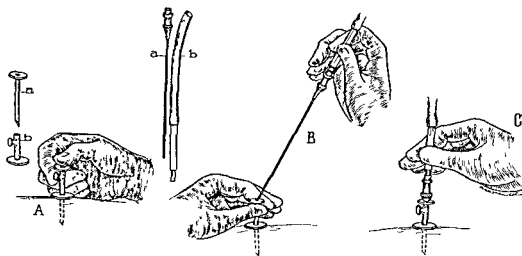


Fig 8—Technic of first induction. *A*, introducing the cannula (*a*) with guard (*b*) adjusted to thickness of the chest wall *a*, Solomon Blunt Needle *b*, observation tube *B*, introducing the Solomon blunt needle fitted with observation tube and rubber connection, *C*, needle in position for insufflating gas.

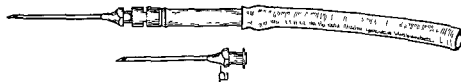


Fig 9.—Reinflation needle (*a*), with observation tube and rubber connection

reinflations, we utilize a 17 gauge Luer needle fitted with a glass observation tube (Fig. 9). In utilizing the Solomon blunt needle and cannula, the danger of gas embolism is best prevented, as will be noted later.

*Gas to be Utilized.*—In spite of arguments to the contrary that carbon dioxide is no safer than atmospheric air, we still feel that it should be used for primary inflation, as it combines with the blood more readily than atmospheric air or oxygen. We are impressed by our personal experience, in which we recorded no accident with carbon dioxide during the past ten years that it has been employed by us for primary inflation; whereas, in the previous ten years in utilization of either nitrogen or atmospheric air, we had two fatal cerebral gas emboli, and nineteen cases presented the picture of pleural reflex. For subsequent reinflations we use atmospheric air.

*Selection of Site for Gas Introduction.*—The possibility of establishing an artificial pneumothorax depends upon finding free pleural space. Unfortunately, many cases exhibiting indications for artificial pneumothorax cannot receive the advantages of the treatment because pleuritic adhesions obliterate the free pleural space. But there is no absolute criterion which permits differentiation in every case between a normal and pathological pleura. The value of the roentgen-ray for this purpose has been exaggerated. The excursion of the diaphragm, even under the fluoroscopic screen, permits no conclusions for, in diffuse lung changes with involvement of the lung border, the phrenicocostal sinus may appear obliterated and lung excursion fail through border adhesions, and yet, offer no real obstacle to gas entry. On the other hand, in cases with lateral adhesions, little interference with diaphragm movement or lung border excursion may take place, yet gas introduction may be impossible. Physical examination undoubtedly gives more trustworthy information than the roentgen-ray regarding the presence of free pleural space, as roentgen films may indicate no adhesions, yet, introduction of air will be found impossible. Generally speaking, the greater the mobility of the lung border, the greater will be the probability of free pleural space. Important hints of existing adhesions are marked weakening of the respiratory murmur over the lower lobe; shortening of the inspiration and demonstration of diminished lung border excursion by percussion or the absence of Litten's sign; however, decision should not be made upon the data gathered from physical examination alone, for one is frequently agreeably surprised in finding a perfectly free pleural space in a clinically adherent one. Even if the case gives a history of previous pleurisy with effusion, which has been allowed to absorb, this does not necessarily mean that the pleural space is obliterated. Consequently, irrespective of physical and roentgenological findings indicating an adherent lung, the only certain method of determining the possibility of establishing a pneumothorax is to attempt it.

As a rule, unless there is evidence of underlying pathology, the 5th or 6th intercostal space, anterior axillary line, is a satisfactory site to attempt the first inflation. On the left side, the position of the heart must be carefully determined and the puncture made well away from it. If no free pleural space is found, a second puncture may be made in the same region, but in the 2nd intercostal space higher; if no free space is found here either, further effort at the first sitting should be abandoned and resumed on the following day, when attempts should be made higher up on the axilla, anterior, in the 2nd and 3rd intercostal spaces in the midclavicular line—also along the posterior axillary line and posteriorly over the lower lobe. If the second endeavor is unsuccessful, quoting from our experience, we have seldom established a satisfactory pneumothorax.

*Preparation of the Patient.*—The patient should be psychically prepared for the operation—that is, the purpose of the procedure should be stated and the patient assured that if the lung is not adherent to the chest wall, the operation will be painless. If the patient occupies a private room in an institution, the primary puncture may be made with the patient resting in bed; but since the most serious accidents are likely to occur during the primary puncture, it is best not to undertake it in a ward—hence, the ward cases can be removed into a dressing room

The use of sedatives and opiates has never been necessary during our long practice.

*Technic of First Induction.*—Establishing a pneumothorax, while a simple procedure, can prove very disastrous, and serious consequences may arise, if an apparently unimportant error is committed. Faulty technic was responsible for many fatalities when pneumothorax made its début. After Saugman introduced the manometer, the most dreaded of all complications, namely, gas embolism, became less and less frequent. With faulty technic, gas embolism is a danger every operator must keep well in the foreground of his mind. This complication will be discussed later.

The patient is placed in bed, or upon a dressing-room table, with the side to be operated upon up, and the head resting without a pillow. The site selected for puncture is painted with iodine or picric acid and alcohol or tincture No. 99 merthiolate 1:1000. A 2 c.c. Luer syringe armed with a two-inch, 26 gauge needle is filled with 1 per cent. novocaine suprarenin solution. A skin wheal is made. Following this, the needle is directed toward the pleura. As the needle is gently pushed into the tissue, the anesthetic solution is injected. One can often feel the needle passing through the external intercostal muscle into the internal one. Caution must be exercised at this point lest the needle be passed through the internal intercostal muscle, endothoracic fascia, parietal pleura and puncture the visceral pleura. If such happens, the patient promptly coughs and air or blood will be drawn into the syringe upon withdrawing its piston. Puncture of the lung may result in a spontaneous collapse or a slow leak. We feel it is much safer to advance the needle up to the parietal pleura and infiltrate the endothoracic fascia; by doing this the pleura will be anesthetized. One then makes a skin stab with a von Graaf knife and pushes the cannula, like a thumb tack, through the chest wall (Fig. 8). When the point of the cannula reaches the parietal pleura, the patient may complain of some pain upon passing through the parietal pleura into the pleural cavity. If the lung is adherent to the chest wall, one will hear (if careful attention is given) a crackling sound coming from the cannula. This always indicates adhesions. On the other hand, if there is free space between the visceral and parietal layers of the pleura, an inward rush of air will be heard as soon as the cannula passes through the parietal pleura. This inrush of air is arrested by placing the tip of the finger over the opening. The Solomon blunt needle, fitted to an observation tube with a short piece of rubber tubing, all three sterile (Fig. 9) is now connected to the pneumothorax apparatus and the needle passed through the cannula into the pleural cavity; the cannula is then pulled from the tissues and allowed to rest outside the chest wall puncture upon the shaft of the needle. The water manometer is now opened, and if the needle is in the pleural cavity, the column of water will oscillate on the negative pressure side of the manometer. Depending upon the apparatus used, as well as the individual patient, this may register from —3 to —6 or even higher. Introduction of gas can be considered safe only if the negative pressure registers at least 3 cm. of water in the manometer, with an excursion of at least 2 cm.

The operator must be thoroughly informed regarding the accidents of gas introduction and the means of preventing them. Following Von Mural's experiments on intrathoracic pressure values, observation of the manometer has become of greatest importance to safeguard the life of the individual. Let it be a fixed rule to introduce no gas before being convinced that the needle is in free pleural space, or before a well defined manometer reading, swinging more than 2 cm. of water and registering, on primary punctures, a negative pressure. Failure to observe this rule may give one a distressing, unforgettable experience and endanger the patient's life. A merely swinging manometer does not indicate free pleural space.

The manometer tells one the position of the needle; if it has entered a bronchus or lung cavity, or air-containing lung tissue, and superficial quiet breathing occurs, with an open glottis, the manometer shows an excursion above and below the neutral point, usually a +1, -1. Upon deep breathing, the variation may be 2 cm. or but very slightly more. One will observe, too, if the patient breathes slowly, that the -2 occurring during inspiration falls to neutral before expiration begins; and the +2 exists only with the beginning of expiration and falls to neutral before inspiration commences. If the patient holds his breath, with the glottis open, either at inspiration or expiration, the +2 or -2 sinks to zero. The explanation, of course, is simple, for pressure variation in air-containing lung tissue, when the glottis is open, exists only during respiratory movement. Furthermore, should gas be admitted, it enters with suspicious rapidity and the patient feels no signs of pressure. Negative pressure readings, with a slightly moving manometer, are also present in case the needle enters a cavity with obstructed opening. Gas entry can cause gas embolism by tearing a small pulmonary vein. Should the needle enter a lung vein, it is said the manometer registers a negative pressure which is increased by deep breathing. Inasmuch as we have never had such an accident in our experience, we cannot verify this. In case a pulmonary artery is entered by the needle, it is reported (we have, likewise, never experienced it) that the pressure is positive and almost stationary, although cardiac oscillations will be noted. If the needle is in solid tissue, the manometer registers slightly negative and no movement takes place. If the needle is in the pleural cavity, the manometer at once shows two characteristics: first, the movement is essentially greater than above mentioned; second, it maintains itself at the end of respiration and does not sink back to neutral, the reading being invariably negative in primary punctures, -3 to -6 or even -5 to -10 c.c. of water; generally speaking, the larger the thorax and the greater the freedom of pleuritic adhesions, the greater the negative pressure. An inverted curve—one that is *plus* on inspiration and *minus* on expiration, occurs in pneumothorax only in paradox diaphragm movement. However, the latter does not always produce reverse pressure values.

The manometer also gives accurate information regarding the presence or absence of adhesions. In case the pressure gradually increases as gas is let in, and no pain is complained of, it speaks for the absence of at least diffuse adhesions, although, on the other hand, if the pressure rapidly goes from neutral to positive, after the introduction of a relatively small quantity of gas, it indicates

adhesions and the patient often complains of pain, referred to the shoulder or stomach, more frequently the former.

*Introduction of Gas.*—After the operator has assured himself, from manometric observation, that the pneumothorax needle is between the visceral and parietal pleura, the stopcock liberating carbon dioxide is opened and gas allowed to flow in. Should pain be complained of, and the negative pressure change quickly to positive after 50 or 100 c.c. of gas has been introduced, one may be certain that adhesions are present, and one should not attempt their separation. Upon the first inflation, we prefer to introduce from 200 to 300 c.c. of carbon dioxide, except in cases where pneumothorax is being instituted to control hemorrhage, when one may use 400 to 500 c.c. or even more. If the introduction of, say, 100 c.c. of gas causes the manometer to register a positive pressure of, for instance, +5, +6, even if the patient complains of no pain, it is best to discontinue the operation for the day.

*Reinflation.*—After two or three days, a gas refill will be undertaken in the same manner as the first inflation—except that the needle through which the anesthetic solution is being injected, instead of halting when the parietal pleura is reached, this time passes through it into the pneumothorax space and gas is aspirated into the syringe to confirm the presence of a pneumothorax. An ordinary 17 gauge Luer needle is now placed on the 2 c.c. Luer syringe and introduced through a stab incision into the pneumothorax cavity. Again, air is aspirated into the syringe to make sure that the needle is between the layers of parietal and visceral pleura. Having confirmed this, the syringe is removed and the sterile observation tube, to which a short piece of sterile rubber is attached, is fitted into the needle and the whole connected with the pneumothorax apparatus. Sterile air may now be used instead of carbon dioxide, as the danger of gas embolism, after the primary inflation, is less likely to take place with careful technic, unless pleuritic adhesions are present and an effort is made to separate them. Ordinarily, the refill may be given in the patient's bed, even in the ward. The site for the refill puncture will be a centimeter, or so, distant from the primary puncture so that in case a pocket is present, it will be entered. Sterile air is then allowed to flow through the needle; a check is made of the manometer reading with the gas stopcock closed after every 50 to 100 c.c. of gas have been introduced. Upon the second inflation, 250 to 300 c.c. of air is used.

*Determination of the Degree of Collapse or Compression to be Maintained.*—While admitting the value of "selective collapse" as well as small volume pneumothorax in some cases, we feel the patient will have greater assurance of a good clinical end result if the lung is fully collapsed and not subjected to changes in volume during inspiration and expiration. Our clinical experience supports our contention that the more complete the collapse is, the better the end result will be.

*Conduct of the Case After the First Refill.*—Subsequent refills will be spaced at longer intervals with larger quantities of gas, so that by the end of the first month, weekly intervals will, as a rule, suffice. In the average case, the intervals will be ten days to two weeks at the end of the third month; they will then be gradually increased until, after a year, the interval will probably run a month to six weeks—depending upon how well the patient retains gas and how readily the

lung collapses. In cases presenting adhesions that interfere with a satisfactory lung collapse, the intervals will be shorter. The interval of refills and quantity of gas to be introduced will be governed by the evidence obtained as a result of clinical observation, laboratory findings and physical and roentgenological examination.

**Control of the Pneumothorax.**—Success, aside from a coöperative patient and a careful selection of cases, requires constant observation of lung changes, absolute knowledge of the character of the pneumothorax and position of the mediastinal contents. This information may be obtained by clinical observation and repeated physical examination. However, persistent study of serial roentgen films made at monthly intervals and fluoroscopic observation, before and after gas injection, are unconditional requisites for every mechanical therapy of lung tuberculosis. It is also important that a careful record be kept of the twenty-four hour sputum quantity measured at monthly intervals, as well as the result of the bacteriological examination of the sputum. No finer guide can be utilized for determining whether the pneumothorax is effectual in cavity cases than the influence of the pneumothorax upon the sputum quantity.

For determining the degree of lung collapse and the character of the pneumothorax, physical diagnostic methods are of little service; this is especially true of the small, flat variety, since neither tympany nor weak breathing can be demonstrated. With a large pneumothorax and a stronger compressed lung, breathing is distinctly weak or absent; râles are faint and distant if existing at all. In case adhesions prevent certain lung portions being entirely cut off from breathing, distinct breathing of a peculiar ringing quality, similar to amphoric breathing is heard through the gas. Râles, if present, have a characteristic metallic sound. On percussion, in total and large pneumothorax, tympany is obtained over the whole hemithorax; also often over the non-collapsed side, due to compensatory changes—so that one can be in doubt as to which side has been collapsed. Auscultation, of course, will plainly certify that the intense, sharpened vesicular breathing is heard over the non-collapsed lung.

Hemorrhage cases are often puzzling. A small, rigid wall-cavity may be a source of much annoyance and continue to bleed because of lack of compression. Stereoscopic roentgen films clear up the difficulty.

Physical signs may indicate complete collapse of the lung, but the roentgen ray will disclose many cases uncollapsed. Numerous interesting and important phenomena are shown roentgenologically that cannot be recognized by any other method; hence, use of the roentgen ray is an absolute necessity to properly inform the operator regarding the character of the pneumothorax.

Rubino has pointed out the importance of noting the diaphragm tonus. This muscle suffers in the wasting process, as do other muscles, particularly the chest muscles; this can be seen especially in women. Diminished diaphragm tonus permits the diaphragm to be pushed downwards as gas is introduced, increasing the intraabdominal pressure. Many patients of the asthenic habitus, especially in the beginning of treatment, complain of fullness of the stomach and loss of appetite, due to downward pressure upon the stomach in left side cases. In

other cases, one observes nausea, loss of weight, insomnia and extreme nervousness. The real position of the diaphragm is only recognizable radioscopically. Brauer designates this symptom complex "vagus dyspepsia" and attributes it to vagus pressure. Reduction of intrathoracic pressure will relieve the condition. The positions of the heart and mediastinum are important. In general, we observe that in cases free of pleural adhesions, and without fixation of the mediastinum, this structure bulges only after the lung is fully compressed, but at times one observes considerable mediastinal displacement after a comparatively slight pulmonary pressure. If adhesions are present, this displacement, at times, appears especially great, making one feel anxious,—yet, the patient rarely complains.

Nitsch,<sup>11</sup> in the Brauer clinic, upon the basis of anatomical studies, has pointed out two weak places in the mediastinum; one, in the anterior mediastinum, between the 2nd and 4th ribs; the other in the posterior mediastinum, in its lower part, between the spine and aorta behind, and the heart and esophagus in front. The former place, being the weaker of the two, often forms an actual mediastinal hernia (mediastinal hernias are clearly seen as halfmoon-shaped areas bulging toward the uncollapsed side). Too great a pressure may defeat the object of collapse by bringing too much pressure on the other lung. Rupture at Nitsch's point is an accident very unlikely to occur.

If mediastinal hernias exist to the disadvantage of the patient, they may be abolished through artificially setting up a circumscribed pleuritis of the hernia, which is followed by a thickening of the mediastinal pleura, resulting in drawing it quickly into its normal position. The technic employed by the author for several years is as follows:

If the anterior mediastinum is the object of approach, one places the patient on a dressing table with the pneumothorax side up. After local anesthesia of an area close to the sternum (but not nearer than 2 cm. because of possible damage to the internal mammary vessels) a 2 c.c. Luer syringe is filled with 1 per cent. gomenol and a 21 gauge needle is placed upon the syringe. The needle is slowly advanced through the chest wall but halts immediately it has entered the pneumothorax cavity. The gomenol solution is slowly injected, with the patient tilted forward so that the solution will run down into the hernia. The needle is then withdrawn and the puncture site covered with a gauze pad and adhesive. The patient remains in the same position for one hour, when a second puncture is made at the same place and 100 c.c. normal saline solution slowly injected in order to float the gomenol. The patient is then placed in an upright sitting position and the salt solution plus the gomenol is aspirated. If the pneumothorax is recent, with a normal pleura, a mild febrile reaction takes place. If no reaction follows, the procedure is repeated after three days, using 2½ per cent. gomenol. Again, if no reaction takes place after the same length of time, one uses 5 per cent. gomenol in repeating the procedure, and, if necessary, 10 per cent. gomenol is employed.

This procedure has been of great service in stiffening the mediastinum in pneumothorax cases, who were candidates for a thoracoplasty, to render them

a better surgical risk by lessening the danger of mediastinal flutter (Figs. 10, 11, 12).

The manometer is an unreliable guide regarding mediastinal displacement since low pressure readings may occur with a thin mediastinal pleura; but, roentgen rays will clearly show the position of the mediastinum and also the

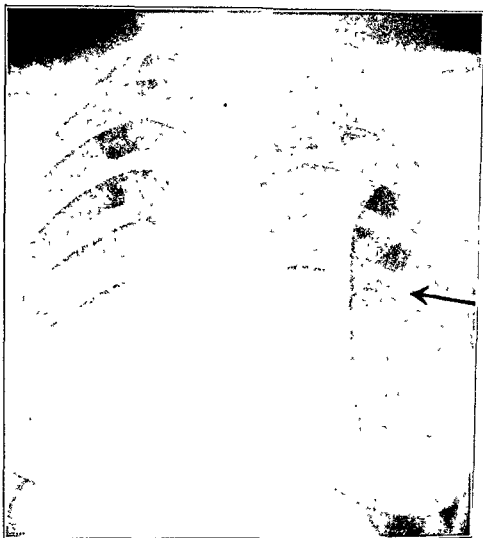


Fig 10—Large cavity uncollapsed because of diffuse adhesion. Tension pneumothorax causing mediastinal herma. The arrow points to a band adhesion. Case referred for pneumolysis.

trachea and heart. In the absence of roentgenological facilities, it is a mistake to collapse the lung until no râles are heard and sputum is no longer expectorated. Often one hears large metallic râles due to the movement of mucus in the large bronchi taking on a metallic quality by resonance in the pneumothorax cavity.

While the roentgen ray is of great value in the selection of cases and in familiarizing oneself with the size and character of the pneumothorax, stetha-



coustic phenomena to detect early damage to the opposite side, must also be relied upon. A careful watch and record of the contralateral lung changes must be kept. After the first few inflations, when the diseased lung has been placed at rest, marked reduction of râles in the contralateral lung is noticed very often as a consequence of a diminution of the resonance phenomenon. Orientation

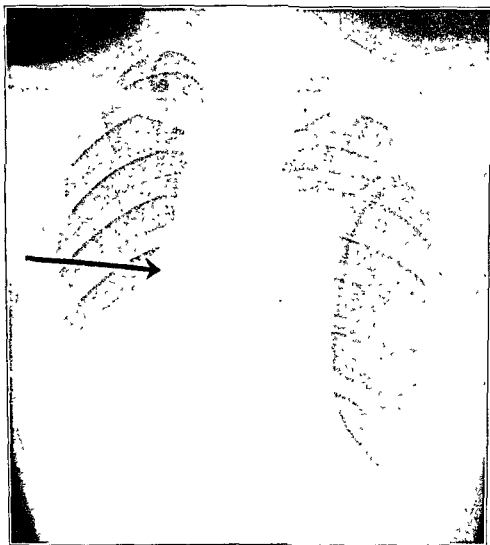


Fig 11—Same case as Fig. 10 one month later. The band adhesion was severed and at the same time oil of gomenol was placed in the hernia, producing a circumscribed pleuritis. Note fluid level in hernia sac and thickened mediastinal pleura.

should be made regarding the character, quantity and extensiveness of râles on the contralateral side, if present, and their topographical location charted at regular intervals—at least monthly. Examination will disclose any increase. In many favorably progressing cases, as a matter of fact, they become less. In case they appear over a wide area, one must either diminish the collapse, leave it off altogether, or consider bilateral pneumothorax.

Regular measurement of the twenty-four hour sputum quantity and germ content is a much neglected but valuable index regarding the efficacy of the pneumothorax. It is obvious that—irrespective of physical and roentgenological findings indicating a satisfactory lung collapse—the collapse is *not* satisfactory if the patient continues to raise a positive sputum in pretty much the same

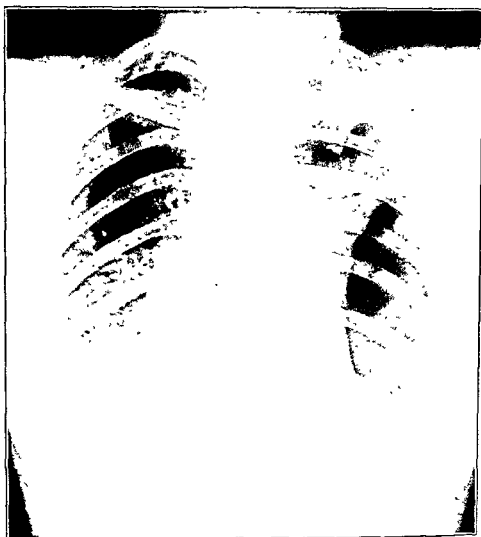


Fig. 12.—Same case as Figs. 10 and 11 two months later. Mediastinum fixed in midline. The cavity was later successfully closed by thoracoplasty.

quantity over a period of several months, provided, of course, contralateral lung sources can be excluded. Needless to say, active collapse or compression should be kept up until the patient is sputum-free. If pleural adhesions or rigid wall cavities do not interfere with the collapse, the patient may be rendered sputum-free in one to three months, and in our experience, if adhesions prevented a satisfactory collapse of the lung, after four to six months' trial, we have found

it best to consider surgical procedures for severing the adhesions, if suitable, or securing a better collapse by other surgical measures.

During the first one to three months, even if the patient is fever-free, bed rest (depending on the case) should be prescribed; following gas inflation, it is customary in our practice to keep the patient in a reclining position with the pneumothorax side up for half an hour during the first month or two. After the temperature has been normal for at least a month, and if the patient's circumstances make it necessary that he become ambulant, leisurely activity may begin, provided there are no contraindications, by allowing the patient to sit up in a lounge chair one hour daily, gradually increasing the sitting-up period to six hours, after which walking exercises may be authorized if no contraindication exists. At first a five minute walk may be indulged in; it may be increased one minute daily, up to twenty minutes. Afterwards, provided all goes well, the sitting up and walking periods may be increased. On the day of the refill, it is best to have sanatorium patients discontinue exercise and rest in bed. All active exertion should be forbidden during the first three or four months of treatment. If, after several months of treatment, the patient is in good clinical condition and forced to work, this is permissible on condition that no physical exertion is required. In most cases refills are then given ambulant, whereupon the patient returns to his occupation.

*Duration of Treatment.*—Much conflicting opinion is voiced concerning this question. We have repeatedly seen excellent recoveries in cases where pneumothorax treatment was carried on six months to a year. However, there will be many relapses with a pneumothorax of so short a duration. By inference from our experience, we feel one should make an effort to maintain the pneumothorax for three years after the disappearance of all constitutional disturbances, including tubercle bacilli from the sputum.

*Discontinuation of Treatment.*—When a decision has been made to discontinue treatments, the intervals between are lengthened and smaller refills given. The patient must be carefully observed and frequently examined, and should any signs of a reactivation of disease be detected, the pneumothorax will be reestablished.

### COMPLICATIONS.

The impression that pneumothorax treatment should be withheld until after a thorough trial of sanatorium methods, and that it should be undertaken with much premeditation because of the danger of complications, is invalid. Less than 2 per cent. of our pneumothorax cases died as a result of complications directly or indirectly related to pneumothorax treatment.

The influence of artificial pneumothorax upon tuberculous complications existing prior to treatment and those occurring during treatment, have been carefully studied by my associates and myself upon 480 patients in the Portland Open Air Sanatorium.

TABLE 1

TUBERCULOUS COMPLICATIONS PRESENT BEFORE TREATMENT AND TUBERCULOUS COMPLICATIONS DEVELOPING UNDER TREATMENT AND INTRINSIC TO THE TREATMENT IN 480 COLLAPSED CASES																				
CLINICAL GROUPS	LEGEND S. Satisfactory Collapse P. Partial Collapse	TYPES OF TUBERCULOSIS	TOTAL CASES	NUMBER COLLAPSED CASES CHARACTER OF PNEUMOTHORAX	NTA CLASSIFICATION		COMPLICATIONS BEFORE TREATMENT		COMPLICATIONS DEVELOPING UNDER TREATMENT											
					II	III	LARYNGITIS	ENTERITIS	SEVERE HEMOPTYSIS	SERIOUS EXUDATE	TUBERCULOUS EMPYEMA	PROGRESSION OF DISEASE OR SITE	EARLY OBSTRUCTIVE PNX.	PLEURAL SHOCK AND GAS EMBOLISM	SPONTANEOUS PNX.	HEMOPHYTOSIS	ENTERITIS	PLEURISY EFFUSION OPP. SITE	EXTENSION OF DISEASE OPP.	LARYNGITIS
1	Fibro-caseous progressive (Little or no excavation)	194	39 S 62 P	41 58 17 45	14 6 7 9	18 17 8 8	4 11 5 4	1 2 0 0	1 4 2 0	0 2 0 0	2 0 2 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0	
2	Fibro-caseous cavernous progressive	177	71 S 70 P	0 71 0 70	11 11 21 13	9 12 7 14	11 5 3 4	0 0 0 0	0 0 2 3	5 3 5 3	4 0 5 3	0 0 3 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0	
3	Fibrocaseous cavernous centy menelationen fore ground	52	21 S 28 P	0 21 0 22	6 5 7 2	5 0 2 6	3 4 4 0	1 1 1 2	0 0 0 0	1 0 2 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0	
4	Severe acute infiltrating caseous pneumonic, etc.	39	13 S 17 P	0 13 0 17	13 3 3 3	2 2 7 2	4 5 4 1	1 0 2 1	0 0 2 2	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0	
5	Tuberculous pleuritis with effusion	20	15 S 5 P	15 0 3 2	0 0 0 0	0 0 0 0	0 0 0 0	0 0 1 0	0 0 0 0	0 0 0 0	0 0 1 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0	
6	Severe and uncontrollable hemoptysis	4	2 S 1 P	2 0 0 1	0 0 1 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0	
7	Bilateral fibro-caseous cavernous	30	7 S 12 P	0 7 0 12	3 3 3 2	1 2 2 4	1 1 1 2	1 0 1 1	0 0 1 1	0 0 1 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0	
8	Desolate bilateral (Ultimum refugium)	84	7 S 58 P	0 7 0 58	7 17 4 18	1 4 6 4	1 0 0 0	1 0 2 2	0 0 0 0	0 0 2 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0	
GRAND TOTAL			600	480	170 310	34 70	68 83	33 34	21 13	16 10	8 7	4 1	1							
1. 29 CASES HAD OTHER MISCELLANEOUS TUBERCULOUS COMPLICATIONS NOT DEPENDENT UPON TREATMENT.																				
2. 9 ADDITIONAL CASES OCCURRED IN "NO FREE SPACE CASES" WHILE ATTEMPTING PNEUMOTHORAX.																				

Table 1 is a summary of the complications in the satisfactory and partial-collapse cases\* in each clinical group. It will be noted that very few cases are

\*The satisfactory collapse group comprises cases wherein pleuritic adhesions did not prevent closure of cavities or adequate functional rest of the lung. Partial collapse cases comprise those wherein pleuritic adhesions did prevent closure of cavities or satisfactory functional rest of the lung.

recorded as having developed tuberculous laryngitis, tuberculous enteritis, and extension or progression of disease in the contralateral lung during treatment.

It must be emphasized that complications tabulated as developing under treatment apply only to those which developed during the actual period of pneumothorax treatment. We, therefore, have not recorded those cases which developed complications after pneumothorax treatment was discontinued. This applied particularly to cases which were favorably influenced, temporarily improved or unimproved and those in which treatment was abandoned. Many of these already had a tuberculous laryngitis or enteritis, and in others the period of pneumothorax treatment was so short that these complications had scarcely time to develop. Many cases undoubtedly developed a terminal progression or extension of disease after suspension of pneumothorax treatment, but they have also been excluded.

Since in the no-free-pleural-space cases only attempts were made to induce a pneumothorax, no complications, except pleural shock or gas embolism, are recorded as having developed under pneumothorax treatment.

**Gas Embolism and Pleural Shock.**—The symptom complex of gas embolism and so-called pleural shock is so similar that at the time of its occurrence, it is sometimes difficult to determine with which of these conditions one has to deal, particularly in cases in which gas has been introduced or the lung parenchyma has been penetrated. The diversity of opinion regarding the question has made it impossible for us to decide which condition occurred in some of our cases.

In over 20,000 inflations we have had 4 cases presenting the symptom complex usually attributed to gas embolism; two of these were fatal. We have observed the symptom complex usually attributed to pleural shock in 19 cases, none of which were fatal. Pleural shock may occur in all degrees of severity. In some of our cases the symptom complex was so alarming that we felt death was imminent.

Our experience with pleural shock and gas embolism has impressed us that they are the most dreaded of all complications arising during the course of pneumothorax treatment. All of our cases of pleural shock or gas embolism occurred in patients in whom adhesions existed. Three cases, however, had a satisfactory collapse; ten had a partial collapse and six had no free pleural space.

Pleural shock may occur at any time during the operative procedure. In some of our cases it occurred during anesthesia infiltration of the pleura—no gas had been administered. In others it occurred during inflation, and in still others, during withdrawal of the inflation cannula after gas had been administered.

In some instances pleural shock developed suddenly with no warning; in many cases it was preceded by a highly suggestive prodromal state. Anesthesia infiltration preliminary to an artificial pneumothorax is usually absolutely painless, but we have observed a marked hyperalgesia and hyperesthesia on the pneumothorax side in several patients who subsequently developed pleural shock. These patients were extremely hypersensitive to the preliminary anesthesia infiltration, complaining of intense pain, not only in the skin but throughout the entire side of the chest.

The earliest symptoms of pleural shock are usually manifested in the facial expression—particularly the eyes, which are fixed, sometimes in a deviated position. Occasionally there is a sudden muscular movement of the patient who makes no reply upon being admonished to remain quiet. A hasty examination will reveal that the patient is already in pleural shock,—either unconscious or, if conscious, unable to talk or control his movements, due to tonic or clonic muscular spasm. Many of these cases are of the convulsive type, closely resembling an epileptic seizure. In other cases, the first warning may be a sudden scream, followed by loss of consciousness with dilated pupils, tonic or clonic convulsions—either general or confined to one part of the body. In two cases in our series (both of whom were nervous, apprehensive women), one came on after an uneventful refill, immediately upon withdrawal of the needle; the other occurred ten minutes after the needle had been withdrawn. Both cases were characterized by psychic symptoms, numbness, loss of consciousness, superficial and irregular breathing, mental confusion, tonic contractions on the pneumothorax side, rapid, weak or irregular pulse, pale skin with cyanotic spots, especially on the face, throat and chest,—though there was no loss of bladder or bowel control. The attacks lasted approximately one-half hour. Recovery without complications took place in both cases. One case was successfully routinely reinflated after a preliminary morphine scopolamine injection. Treatment was discontinued in the other case because of the temperament of the patient, who was six months pregnant.

In order to detect the very earliest manifestations of pleural shock, our patients are always placed in the most comfortable position and requested to make no sudden movement. The face is kept in full view; the eyes are carefully watched for any suggestive symptoms. Attention to these precautions will enable one to administer early treatment and frequently avoid serious consequences.

A careful study of all our cases of pleural shock and gas embolism has been made—copious notes having been taken during the actual occurrence of the phenomena; but, a review of the clinical bedside notes reveals no uniformity of symptoms by which we can sharply differentiate between pleural shock and gas embolism at the time of the accident.

To avoid pleural shock, apprehensive or hypersensitive patients should be mentally prepared and during the inflation one should be constantly on the alert. In individuals of this character, we have seen the symptom complex, closely similar to that of pleural shock, occurring in various degrees of severity at the time of each reinflation, which, along with other stigmata, convinced us that it was purely hysterical.

Gas embolism may result from lung puncture, with no gas having been released from the apparatus. Brauer, Spangler, and Saugman have pointed out that alveolar air is slightly positive, while the venous pressure is negative during inspiration, and, as Brauer states, if the vein is stiffened by a tuberculous infiltration, air embolism may result from a lung puncture—the needle establishing a communication between the vein and alveoli or between a bronchus and the vein.

After a fatality from gas embolism occurring during inflation, adhesion cases are approached with much timidity. One hesitates to introduce gas in a case showing a slight manometer excursion, indicating an adherent pleura; and yet one is tempted to, because of the feeling that the needle outlet is resting between the pleural surfaces and that they might separate, as they often do, following gas introduction. In such cases, it has been our custom to attempt separation of the pleural surfaces by introducing normal salt solution through the pneumothorax needle. There is no danger of gas embolism in the introduction of salt solution for the purpose of finding free pleural space, and very often the pleural surfaces separate, permitting subsequent gas introduction. In case inadequate free space is produced to justify even a partial collapse with air, we frequently introduce hypertonic salt solution (25 to 10 per cent) into pockets between the pleural surfaces. This causes an inflammatory reaction, the severity of which can be regulated by the strength of the salt solution; subsequently, proliferative inflammatory changes take place, followed by marked pleuritic thickening, and still later, retraction, which serves to lessen respiratory movement and rests the diseased side. This method, we believe, is of value not only in avoiding gas embolism, but as a therapeutic procedure in cases wherein adhesions prevent establishing a pneumothorax. We have never had a gas embolism or pleural-shock symptom complex occur when we followed this procedure. We have also used the method to produce retraction changes prior to thoracoplastic operations.

If a fixed rule were adopted never to introduce gas until the manometer shows a correct reading, gas embolism would invariably be avoided. Still, in spite of every precaution, it may take place while the operator is maneuvering the needle, seeking a suitable manometer excursion. Under these circumstances, the accident could happen as a result of leaky apparatus permitting gas to escape from the apparatus which is supposedly shut off. Such a mishap should never occur if all stopcocks are leak-proof. Gas embolism caused by the pneumothorax needle entering the lung and establishing a bronchovenous fistula, is more difficult to avoid. Even in this event, if a blunt needle is used for the primary inflation, and if upon reinflation with a sharp needle, one makes sure its point rests within the pneumothorax space previously established, accident should be avoided. In either case, no gas must be allowed to pass from the apparatus until the manometer gives a proper reading. We are certain that carbon dioxide is safer for primary inflation for the reasons already stated.

**Serous Exudate.**—This complication may occur soon after pneumothorax treatment has been started, or it may develop after months or even years of treatment. Its clinical picture is extremely varied but three types stand out prominently.

One form comes on benignly; the effusion forms slowly and has little tendency to increase; there is little or no fever and unmarked constitutional disturbance, unless considerable fluid forms, when the patient complains of dyspnea. It has a tendency to disappear, then reappear after a few weeks or months, and frequently is discovered only as a result of routine radioscopic examination. Unless it forms in quantities sufficient to change the intrapleural

pressure, there is no necessity of aspiration. Should it form in considerable quantities, it is best to aspirate it at the time of a gas refill. The fluid in this type is of a clear straw color and contains almost no organized elements.

In the second form, the patient complains of slight elevations of temperature, anorexia, and pain, aching, or tiredness in the chest. Radioscopic examination reveals fluid. In one case, the constitutional disturbance may be present for a few days, and later the fluid disappears. In another case, the constitutional disturbance lasts for several weeks, or months, and fluid continues to form, requiring aspiration and air replacement. Eventually it disappears, possibly followed by oblitative pneumothorax. The fluid in this type is clear at first but becomes turbid and often frankly purulent. Animal inoculations will almost invariably prove positive. This type should be treated by aspiration and air replacement, but when it assumes a purulent character, irrigation with salt solution, or Dakin's solution, or oleothorax should be considered.

A third form frequently occurs following cold, exposure or intercurrent respiratory infections. It is sometimes seen after abdominal operations or childbirth, and begins with a sharp elevation of temperature, often with pain or a feeling of tightness or aching on the pneumothorax side, the patient being visibly ill. Radioscopic examination may not reveal fluid for the first few days. After it forms the temperature abates, provided it is a pure serofibrinous exudate. This form rapidly becomes purulent and animal inoculations are always positive. If aspiration and air replacement (although aspiration should be deferred until after the acute picture has subsided) do not bring about an improvement, washing out the pleural cavity with salt solution or Dakin's solution should be carried out. Oleothorax should also be considered when frank pus forms. This latter type of exudate is probably due to the extension of a tuberculous lung focus into the pleura. It is very often followed by pleuritic thickening and, later, by oblitative pneumothorax.

Of our 480 collapsed cases included in this study, 83 developed a serous exudate in amounts of 50 c.c. or more. We believe that nearly all cases develop an exudate at some time during their pneumothorax treatment if the pneumothorax is maintained long enough; but, the quantity may be so small as to escape detection, unless especially sought. The exudate may fill only a portion of the phrenicocostal sinus; it may be transitory in character (lasting but a few days), and may be productive of no clinical symptoms. Serous exudates may follow the separation of adhesions, but we doubt whether this is the usual cause. The mere presence of gas in the pleural cavity acting as a foreign body and the unphysiological intrapleural pressure conditions are sufficient to produce an exudate.

**Purulent Exudate.**—While it is apparent from the foregoing that purulent exudate may begin as a serous exudate—either benignly or with a stormy onset—and that the borderline between many so-called serous exudates, having slightly turbid fluid and an early purulent effusion is not clearly demonstrable, undoubtedly many serous exudates are potential empyemas. We have repeatedly seen cases wherein the fluid remained clear for months, then became purulent.



Purulent exudate is a much feared complication by most pneumothorax patients; yet, the complication is not always to be regarded as a serious affair. One sees cases with thickened pleura, with large quantities of purulent exudate, entirely free of constitutional disturbances. Acute and subacute flare-ups, however, are not uncommon and require bed rest. In some of these cases the exacerbation does not recede; the patient gradually loses ground, with extension and progression of disease, terminating fatally.

Purulent effusion may *begin* as a benign exudate, which, after weeks or months, gradually becomes purulent; little constitutional disturbance may accompany it. After a few aspirations, effusion disappears.

A *second type* begins with fever, chest pain, anorexia and so forth. At first the fluid is clear, then becomes purulent after a few days or weeks. In spite of aspiration and irrigation, there is little tendency for it to disappear; it may continue for months or years, and yet when the constitutional disturbance at the onset has disappeared the patient is able to resume work and be treated ambulantlv by aspiration and oleothorax.

A *third form* of purulent exudate is ushered in acutely with high fever, severe constitutional disturbances, and early appearance of frank pus; the temperature keeps up with rapid decline of the patient's condition, unless urgent treatment is immediately instituted.

**Empyema.**—There were 59 cases (12 per cent.) of tuberculous empyema in our 480 collapsed cases. This number included some patients who presented themselves with a tuberculous empyema associated with a spontaneous pneumothorax and also included all those cases which we designated as *sterile empyema* early in our work.

Our observations during recent years have verified beyond any doubt that nearly all purulent exudates complicating artificial pneumothorax are tuberculous in character: we have been able to demonstrate this by animal inoculation. Tuberculous empyema usually arises from ulceration of a superficial caseated focus into the pneumothorax cavity or as a result of spontaneous pneumothorax. Tearing a portion of the lung cortex in attempts to stretch adhesions, thus exposing tuberculous foci, is also a cause.

In the 59 cases developing empyema it occurred just as frequently in the partial-collapse cases, in which adhesions were necessarily under tension, as in the satisfactory-collapse cases, in which they were not necessarily so (12 per cent. of each).

The manifestation of empyema in each clinical group was very much in proportion to the duration of the pneumothorax and the intensity of the disease; the longer the maintenance of the pneumothorax and the more widespread the disease, the more frequently was empyema a complication. It naturally follows that the longer the pleural surfaces are separated and the more progressive and widespread the disease is, the greater will be the opportunity for infection of the pleural cavity by the breaking down of tuberculous foci. Contrariwise, if the pleural surfaces are in contact, protective adhesions form and prevent infection of the pleural cavity, except, of course, in those

cases in which spontaneous rupture of a superficial cavity takes place following physical exertion or coughing, sneezing, etc.

It is important to aspirate a tuberculous empyema early,—the aspiration often to be supplemented by irrigation with normal salt solution or Dakin's solution, if necessary; since danger of lung perforation is enhanced by a long-continued presence of the empyema, an effort to effect its early permanent disappearance

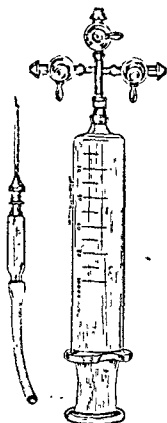


Fig 13.—13-gauge needle and observation tube of same caliber and rubber tubing and 100 c.c. Luer syringe with author's three-way stopcock.

is important. In cases failing to clear up by aspiration, or by aspiration and irrigation with normal salt solution, we have employed Dakin's solution and find it commendable. If the desired results are not produced by aspiration and irrigation with salt solution or Dakin's solution, oleothorax ought to be considered.

*Drainage.*—A rib resection ought to be resorted to only after repeated aspiration and failure of closed tube drainage, but it is seldom necessary, except where the pus is too thick to aspirate or drain by the intercostal method. Rib resection may also be necessary when it is found that entering the pleural cavity with a needle is difficult because of the narrow intercostal spaces and thickened pleura, and adequate drainage cannot be established by the intercostal route.

The drainage must be airtight and placed at the floor of the pneumothorax cavity so that no residual pus will be retained. Of our 59 cases of tuberculous empyema, we resorted to airtight tube drainage with constant suction under slight negative pressure in 5 cases, with two complete recoveries and three deaths. Three other cases that had developed an empyema passed from our observation. They had been operated upon elsewhere by the ordinary open method, and we learned later that all had terminated fatally. Three additional cases residing at remote points (but now in our clinic) were also operated upon elsewhere by the open method and are still living but will require radical thoracoplastic procedures to obliterate their pneumothorax cavities.

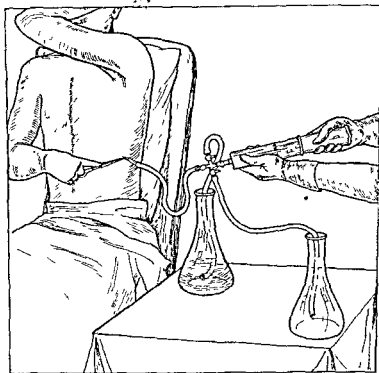


Fig. 14.—Method of aspirating and washing out the pleural cavity and replacing with other fluids or air.

*Technic of Aspiration.*—Instead of the Potain apparatus, we use a 100 c.c. Luer syringe with a three-way stopcock\* for aspiration with air replacement (Fig. 13). This assembly surpasses any other equipment, as the three-way stopcock, which I have designed, enables one to aspirate pus rapidly, evacuate it into a container and replace it with air or salt solution at once; this requires little or no change in the intrapleural pressure. After washing out the pleural cavity with salt solution, if one wishes to introduce other substances it is done very conveniently and without any contamination with pus. As each 50 to 100 c.c. of pus is withdrawn, it is immediately replaced with air. In this way, the intrapleural pressure and its influence upon the lymph and blood stream is so slightly altered that there is no reaction.

\*Manufactured by Becton, Dickinson & Co, Rutherford, N. J.

If the pleural cavity is to be washed out with salt solution, we aspirate the pus, replacing it with air as each 100 c.c. of pus is removed. After the pleural cavity is free of pus, salt solution is introduced 100 c.c. at a time and 100 c.c. of air aspirated. After several hundred cubic centimeters of salt solution have been introduced in this manner, the patient, if his condition jus-

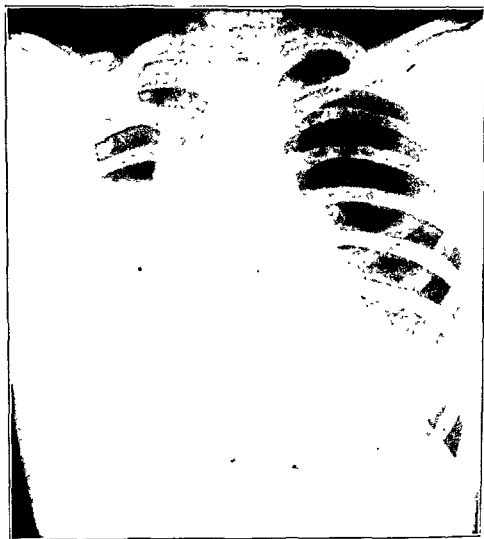


Fig. 15.—Acute tuberculous empyema. Temperature 102°—103° F. Weight 140 lbs. Ill two months. Treated by aspiration and irrigation with air replacement. Pneumothorax continued two years.

tifies it, is turned about in various positions in order to wash débris from the walls of the pleural cavity; aspiration is then carried out and replacement with air made in the manner mentioned (Fig. 14), and the case continued with air inflation for the required length of time, depending upon the underlying pathology (Figs. 15 and 16).

Elias<sup>12</sup> claims, in his report in 1925, covering several years experience, to have been the first to utilize aspiration and air replacement in the treatment of thoracic empyema. But we have used this procedure routinely since 1910, and I am certain that other American workers employed this method at about the same time.

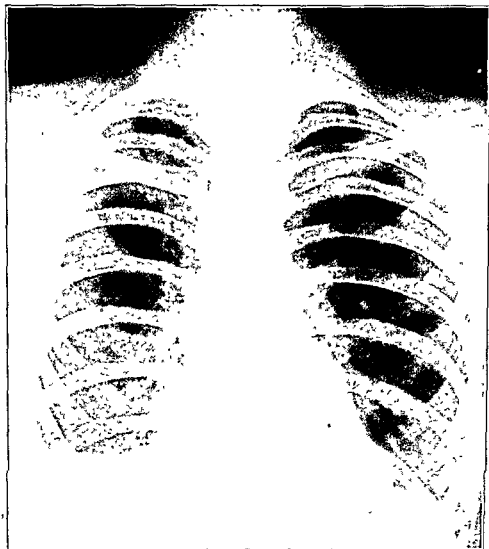


Fig. 16—Same case as Fig. 15 three years later. Right lung fully expanded. Weight 168 pounds.

If the above method is not sufficient to control temperature and keep the pleural cavity essentially free of purulent exudate, it should be washed out thoroughly with a large amount of normal salt solution or 1 per cent. Dakin's solution. This is best accomplished by introducing two 13 gauge needles, one at the upper limit of the empyema cavity and one at the lower, placing the needles in such a manner that the irrigating solution is introduced at one point, washing

the entire cavity and passing out through the other needle (Fig. 17). By this method, 5000 to 10,000 c.c. of irrigating solution may be run through the pleural cavity at one sitting. Frequently a few such irrigations are sufficient to control temperature, after which one can again resort to simple aspiration, etc. (Chart I).

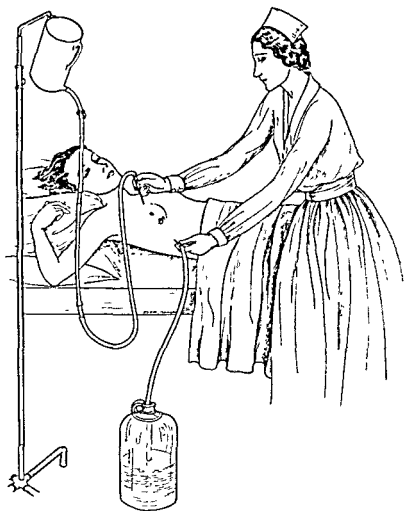
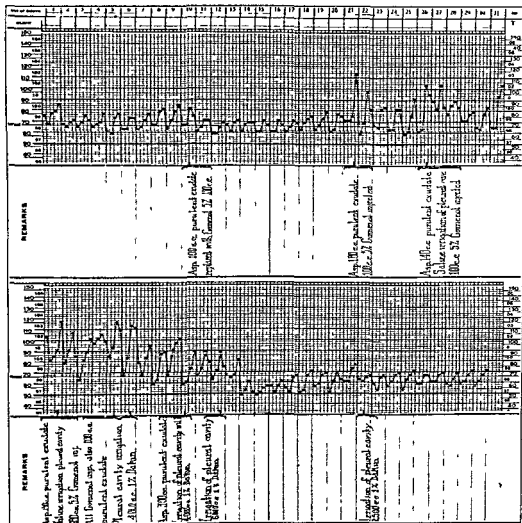


Fig 17.—Method of washing out pleural cavity in cases wherein large quantities of fluid are used

If, in spite of such conservative treatment, the temperature and purulent exudate formation remain uncontrolled, a closed tube intercostal drainage should be established, and after the acute stage, the Carrel-Dakin treatment begun. For irrigation, this treatment is particularly valuable in preventing chronic empyema because of its solvent action on the organized fibrin and lymph which forms on the visceral pleura, causing thickening and preventing expansion of the lung. If a bronchopleural fistula is present, the Carrel-Dakin treatment is contraindicated because it is irritating to the bronchial mucosa and provokes coughing paroxysms. Furthermore, it prevents healing of the

CHART I



fistula by dissolving the fibrous plug, often closing it. Saline solution may be used for irrigation, if a bronchopleural fistula is present, but it should be employed cautiously as a coughing paroxysm, which is often provoked immediately when irrigation is begun, may not be incited until the pleural cavity contains a considerable amount of salt solution, at which time this and purulent material may be suddenly spilled over into the other lung during coughing, causing aspiration pneumonia.

**Tuberculous Laryngitis, Enteritis and Other Tuberculous Complications.**—In spite of the fact that 94 cases had a well-defined tuberculous laryngitis before treatment, only one case developed laryngitis under treatment and compelled us to abandon the pneumothorax. According to our experience, tuberculous laryngitis does not contraindicate pneumothorax treatment unless its severity interferes with the patient's nutrition. On the contrary, improvement takes place along with improvement of the lung and is often dependent upon it.

*Tuberculous Enteritis.*—This is a serious complication, and when so severe as to interfere with the proper nutrition of the patient, a pneumothorax is seldom justified.

We appreciate the fact that nearly all cases of open pulmonary tuberculosis have an infiltration of the lymph follicles of the intestines which may not be productive of symptoms, but 70 of our collapsed cases presented a well-defined symptom complex of tuberculous enteritis, and its presence was confirmed by physical diagnostic or roentgenological methods. In 17 of our collapsed cases its progression caused us to abandon pneumothorax treatment. In 7 of these, the complication appeared after beginning pneumothorax treatment.

*Spontaneous Pneumothorax.*—In our series of 480 collapsed cases, 16 (approximately 3 per cent.) developed a spontaneous pneumothorax into the pneumothorax cavity; it was fatal in 3 cases.

Because some cases do not display symptoms, and they are so mild in others as to be attributed to other causes, spontaneous pneumothorax or lung perforation into the pneumothorax cavity occurs with greater frequency than is generally recognized.

The perforation may be so small that only a slow leakage of air is permitted, probably instigating no subjective symptoms. At times, the only absolute evidence of perforation is obtained from the manometric readings. The symptoms are largely dependent upon the size of the pneumothorax cavity, the presence or absence of adhesions or exudate, and the size and character of the perforation—that is, whether of the valve type or not.

Although our series of lung perforations is small and justifies no conclusions, we feel, as regarding the case of empyema, that the most frequent cause of perforation is the breaking down of tuberculous foci in the lung cortex.

While 10 of our 16 cases occurred in partial-collapse cases, in which stripping off a portion of the lung cortex or tearing the wall of the cavity may have been etiological factors, we believe that the perforation even in these cases is chargeable to the ulceration of a superficial caseous focus (as in the case of empyema), or to sudden rupture of a superficial cavity.

Physical strain—particularly coughing paroxysms—may cause lung perforation, since it may occur as a sequel to any condition that suddenly produces a great increase in the intrapleural pressure. The lung was ruptured in two of our cases following coughing, and in four during or after physical strain. Two of these occurred while straining at stool.

Puncture of the lung at the time of inflation may be followed by lung perforation, especially if one uses a sharp-pointed reinflation needle.

Not all cases of spontaneous pneumothorax into a pneumothorax cavity are associated with the formation of exudate. The majority, however, are soon followed by an exudate, that may at first be serous, quickly becoming turbid, then purulent or mucopurulent.

When the rupture of a cavity into the pneumothorax cavity takes place, the patient may suddenly fail to raise the usual amount of sputum, or expectoration



may cease altogether, for the reason that the sputum is draining into the pneumothorax cavity.

The size of the spontaneous pneumothorax will depend upon the extent and character of adhesions, if present. Those in which adhesions permit only a localized spontaneous pneumothorax offer a much better prognosis.

*Hemoptysis.*—*Preceding, or shortly before pneumothorax treatment, hemoptysis was present in 82 cases. It developed during treatment in 10 cases. Aspiration tuberculosis, as a result of hemoptysis, developed in two cases; in both instances it was fatal.*

*Early Obliterative Pneumothorax.*—Under ordinary circumstances, obliterative changes ultimately develop in all pneumothorax cases—the time required for completion varying within a wide range. We have been successful in maintaining compression in some cases for periods exceeding six years.

A study of our records shows that out of 245 partial-collapses the pneumothorax was maintained for less than six months in 149, yet even these short periods of inflation have been productive of beneficial results; because the obliterative process took place in the usual manner, these cases are not designated *early obliterative pneumothorax*. But, in 21 cases, as a result of proliferative inflammatory changes with organization of exudate and dense pleuritic thickening, it took place with such unusual rapidity that we have classed them as *early obliterative pneumothorax*. In two cases the tuberculous process was progressive and terminated fatally.

*Pleurisy with Effusion on the Noncollapsed Side.*—This interesting and unusual complication occurred 7 times among our 480 collapsed cases. In one case, the noncollapsed lung had a deep peribronchial infiltration; four had active fibrocaseous infiltrations; one had a disseminated bronchogenic caseous extension, and one occurred in a bilateral fibrocaseous cavernous case. In five of the cases there was a partial pneumothorax on the collapsed side, and in two, the pneumothorax was satisfactory.

*Surgical Emphysema.*—Two types of surgical emphysema are seen—the superficial and deep. Superficial emphysema involves the tissues of the chest wall and, at times, the neck and face, and is almost entirely avoidable. It is seen in the following instances: when large needles have been passed through a thick, rigid pleura, resulting in leakage from the pneumothorax puncture; when high intrapleural pressure is resorted to; and when coughing follows a refill. Tight strapping with a pad over the site of puncture will prevent or control this complication.

Deep emphysema may involve the mediastinum or the inner chest wall. In the former case, gas may reach the mediastinum by passing through the interstitial lung tissue to the hilum. If gas is present in sufficient quantities to exert considerable pressure upon the trachea or large blood-vessels, this complication may be alarming.

Emphysema of the inner chest wall takes place as a result of gas passing along the endothoracic fascia. It may be found over the pleural cupola or even in the neck.

*Miscellaneous Tuberculous Complications.*—These occurred in 29 cases and included several of urogenital tuberculosis, one of which was fatal, and one tuberculous meningitis which was fatal.

In our series of cases, we have had no accidents such as puncture of the heart or pericardium, puncture of the peritoneum, extensive surgical emphysema, mediastinal or interstitial emphysema. As a matter of fact, with technic developed as it is today, fear of their occurrence is greatly reduced.

### PLEURITIC ADHESIONS.

In establishing a satisfactory compression, adhesions proved to be the greatest obstacle. They were of such character in 120 cases that after repeated attempts, no free pleural space was found. In 245 cases, on account of adhesions only a partial compression could be established; even in our satisfactory compressions, adhesions were encountered in a great majority of the cases, but their character did not prevent the establishment of a satisfactory compression.

As a result of our observations, we believe that no tuberculous lung, diseased to the extent of demanding a pneumothorax, is wholly free of adhesions. They are almost regularly present in varying degrees of fixation over cavities, attaching the diseased lung to the chest wall.

Adhesions may be encountered and cause interruption of compression at any phase of pneumothorax treatment. When they are preventing a satisfactory compression, treatment should be energetically carried on by very frequent inflations, extreme caution being exercised to avoid too high pressure, which might precipitate a tear. If unsuccessful, after four to six months' endeavor to establish a satisfactory collapse, one should consider severing the adhesions instead of continuing a useless pneumothorax.

A careful study of roentgenographs shows that nearly all of our cases of upper lobe tuberculosis had apical adhesions. In many instances, early in our work, we advocated separation or to stretch them into long bands, so that they did not interfere with a satisfactory compression, but in some cases they were so firm that separation or stretching could not be accomplished with safety and even though a good compression was apparently present, a study of stereoscopic plates revealed that the upper portion of the lung was only flattened against the upper mediastinum. Thus, cavities were only pressed into an elongated form, the apical adhesions preventing their contraction.

Efforts to establish a satisfactory collapse of the lung by separating or stretching adhesions is a practice we have entirely abandoned in favor of other methods which will be discussed later.

With a good compression and an essentially negative contralateral lung, unwavering stability of a positive sputum should lead one to search adhesions at the apex and in the costovertebral gutter. The anatomy in the region of the summit of the lung and costovertebral gutter is such that these adhesions are not always visible upon a flat plate, but are readily seen on stereoscopic or lateral films. A further discussion of adhesions will follow in the next chapter.

# INFLUENCE OF ARTIFICIAL PNEUMOTHORAX ON TUBERCULOUS LESIONS IN THE CONTRALATERAL LUNG.

The indications and contraindications for collapse therapy are specified quite explicitly as far as the lung is concerned wherein most widespread inroads have been effected by disease.

A marked disparity of conviction prevails, nevertheless, regarding the influence of a pneumothorax upon tuberculous foci in the contralateral lung. It is especially directed to the amount and character of disease that will tolerate a collapse of the opposite lung with safety and a propitious result.

Motivated by this broad difference of opinion relative to the latter question, my associates, Drs Ray W. Matson and Marr Bisaillon, and I,<sup>13</sup> with great care and diligence analyzed a group of 423 cases of pulmonary tuberculosis subjected to artificial pneumothorax treatment.

Only chronic types of tuberculosis are embodied in this analysis of 423 cases, particularly the fibrocavicular and fibrocavicular cavernous groups. Since more discriminating observations of these are possible, they can be studied for longer continuous periods than acute forms of tuberculosis and those cases in which the collapse was executed merely as an extenuating measure to control severe symptoms, hemoptysis, etc.

The 423 cases were classified into the groups given in Table II. According to the National Tuberculosis Association classification, 358 cases were far advanced and 65 cases were moderately advanced.

TABLE II

	Cases
Chronic fibrocavicular tuberculosis, progressive, with little or no demonstrable excavation	194
Chronic fibrocavicular cavernous tuberculosis, progressive	177
Chronic fibrocavicular cavernous tuberculosis with cavity manifestations in the foreground	52

Since the end-results of pneumothorax therapy are associated with and dependent upon the behavior of the contralateral lung, if accurate deductions based upon a comparison of end-results are to be made, it is essential that a classification of the status of the opposite lung be adopted. Thus, there will be more possibility to appraise decisively the prognostic significance of the various types of contralateral lung disease before collapse therapy is utilized. Those cases subjected to pneumothorax usually presented a dominant type which we classified as shown in Table III.

**Description of Classification.**—1. *Essentially Negative.*—We have classified as "essentially negative" those cases in which the physical and roentgenological findings were well within the limits of normal disparity.

2. *Deep Peribronchial Infiltration.*—The outcome of physical examination, in general, is essentially negative, aside from suspicious breath-tone changes with no moisture. The diagnosis is based upon roentgenological findings and is characterized by a pronounced increase in the bronchial tree shadows, particularly those shadows which radiate from the hilum toward the superficies. They customarily have the appearance of an anomalous, beady or varicose arborization,

TABLE III  
END-RESULTS IN 423 CASES OF FIBROCASEOUS  
AND  
FIBROCASEOUS CAVERNOUS TUBERCULOSIS

Status of Contralateral Lung	No. of Cases	Character of Collapse	No. of Cases	Clinically Well		Arrested		Dead	
				Number	Per Cent.	Number	Per Cent.	Number	Per Cent.
Essentially negative	97	Satisfactory	56	29	52	11	20	8	14
		Partial	25	10	40	1	4	6	24
		No free space	16	4	25	1	6	9	56
Deep peribronchial infiltration	103	Satisfactory	49	24	45	12	24	10	20
		Partial	33	3	9	7	21	20	60
		No free space	21	1	4	3	13	9	43
Disseminated bronchogenic caseous extension	40	Satisfactory	15	4	26	4	26	5	33
		Partial	21	1	4	5	24	14	66
		No free space	4	0	0	0	0	3	75
Active fibrocasseous infiltration	134	Satisfactory	50	24	48	11	22	11	22
		Partial	59	4	6	12	20	27	45
		No free space	25	0	0	3	12	19	76
Quiescent fibrocasseous infiltration	49	Satisfactory	21	10	50	5	24	4	20
		Partial	16	4	25	6	37	6	37
		No free space	12	2	16	2	16	4	33
	423		423	120		78	..	155	..

with fuzzy or clear-cut borders, depending upon the age and activity of the lesion.

Roentgenological findings of this character, when the other lung is definitely tuberculous, vindicate the diagnosis of deep peribronchial tuberculous infiltration, without further question.

From the standpoint of pneumothorax therapy, the peribronchial type of tuberculous infiltration *per se*, is not a contraindication as long as it remains confined to peribronchial structures.

In lesions of this type, there is a tendency to invasion of lung parenchyma, and when that takes place, it becomes a serious matter indeed, especially if occurring during the course of pneumothorax treatment.

When the lung parenchyma is involved, it will be usually demonstrable by physical diagnostic methods and its evolution may be followed by the study of serial roentgen films.

3. *Disseminated Bronchogenic Caseous Extensions.*—These lesions, so constant in the study of gross pathological changes, usually occur as a result of the aspiration of bacilli-laden sputum into the contralateral lung, and are characterized by the presence of localized caseous pneumonic, caseous bronchopneumonic and disseminated confluent tuberculous infiltrations, frequently associated with a tuberculous bronchitis. These bronchogenic extensions usually take place into the dependent portions of the lung or into the perihilar region. Roentgenologic-

ally, they are revealed as disseminated patches of increased density, corresponding to the distribution of the lesions and varying in character according to the activity or inactivity of the process. If deep-seated, they may escape physical diagnostic procedures, but if superficial they are readily recognized by the continual presence of moisture and alterations in breath-tones.

4 and 5. *Active and Quiescent Fibrocaseous Infiltrations.*—These lesions, in contradistinction to the bronchiogenic infections above described, usually occupy the upper half of the lung. They are readily recognized by the usual physical diagnostic and roentgenological procedures, although there is a frequent disproportion between physical and roentgenological findings, and to place sole reliance upon one or the other alone will frequently lead one astray. The activity or inactivity of the process is determined by a correlation of these findings. The presence of moisture does not always indicate activity, although its absence by no means indicates quiescence.

**Selection of Material and Control of Treatment.**—The recognition, interpretation and classification of these various lesions in the opposite lung are of paramount importance in the selection of material, and great caution should prevail in their treatment.

As a result of the observations made during the treatment of some of these last-resort cases, we realized that excellent results could often be obtained, even with extensive invasion of the opposite lung. Occasionally a complete restoration to normalcy was even possible, although it must be admitted that this eventuation was contingent on numerous elements, such as the character of collapse, flexibility of mediastinum, type of opposite lung lesion, and surveillance of any changes occurring therein.

We have noted that a diseased lung differs enormously in its reaction to collapse of the other side. Certain types of contralateral lung disease can be approached with comparative security, while in others approach is made with much trepidation and anxiety.

The fibrocaseous lesions located around the root of the lung, or the bronchiogenic caseous extensions scattered throughout the lower portions of the lung react much less favorably as a general rule than the fibrocaseous lesions involving the apex or upper portion of the lung.

The variance may be accountable to upper-lobe lesions being more firmly immobilized by fibrosis and pleuritic thickening and are usually favored with better drainage, while lower-lobe lesions are unfavorably influenced by being subjected to greater amplitude of respiratory motion, in this way inhibiting fixation and favoring aspiration of sputum and dissemination of disease, which are further enhanced by poorer drainage.

Moreover, cardiac activity causes incessant motion in certain types of lesions. This is particularly true in the perihilar region.

All patients reported in this series received sanatorium treatment, and many had exhausted various climatic, dietetic and hygienic procedures. In a number of cases, the delay promoted formation of adhesions, which frequently prevented the introduction of gas. We now believe that, if after a brief period of observation (one to three months), any doubt exists as to the favorable outcome by the

usual sanatorium regimen, collapse therapy should be immediately instituted—if there are no contraindications. This application is especially indicated in cavity cases with copious expectoration, for it is in these that there is most danger of metastatic spread to the opposite lung, larynx or bowel, and a pneumothorax must be established at once. Tardiness in utilizing pneumothorax treatment caused many failures through the development of these various complications.

However, if the contralateral lung lesion is very active, it is better to allow the activity of the process to subside somewhat before resorting to collapse therapy. If the disease in the contralateral lung is not too active, this danger can be minimized by interposing a thin layer of gas, thus separating the worse diseased lung from the chest wall to the extent of an inch or two, and then maintaining this character of collapse while observing the changes of the opposite lung. We have frequently noted the commendable effects of these small degrees of collapse, not only in the worse diseased lung, but also in the contralateral lung, especially in the fibrocascous lesions involving the upper portion. In many cases this technic has enabled us to bring about a gradual satisfactory collapse of the worse diseased lung, with an unhindered improvement of the opposite lung process, even leading to complete recovery. In some cases, prolonged collapse has had no appreciable influence on the opposite lung process; in others, progression of disease took place in the opposite lung. In still other cases, the contralateral lung lesion remained stationary for years, later on becoming rapidly progressive and demanding a pneumothorax (Figs. 18, 19, 20).

After the indications for collapse therapy of the worse diseased lung have been established, there yet remains the task of estimating the integrity of the opposite lung, for, after instituting a pneumothorax, one may be confronted with the problem of whether or not derogatory symptoms are resulting.

To determine this, accurate records of the status of the contralateral lung are necessary. These records should contain the exact topographical distribution of physical findings recorded before each inflation and as often as necessary during the interval. Râles should be studied and the following points carefully noted: whether they appear only on expiratory cough or on the first inspiration following, or whether they are present on ordinary breathing. Their character, amount and true anatomic distribution should be chronicled, so that the record can be compared with all previous examinations. The roentgenological control must be carried out with great frequency.

*Fluoroscopic Examination*—It is our custom to make a fluoroscopic examination from which an orthodiagram is prepared before each inflation; also, during the early phases of the collapse, the fluoroscope must be resorted to more frequently in order to determine the amount of gas to be introduced, and the proper interval for inflation.

The reaction of the lung to inflation and absorbability of gas will depend on each individual patient.

Unless the fluoroscope is employed liberally, the integrity of the contralateral lung may be threatened after the first few inflations, owing to undue functional activity upon it by excessive displacement of mediastinal contents, which might otherwise escape detection. It is not advisable to rely solely upon

manometric pressure readings and physical findings to determine the character of collapse, as has been stated.

In the roentgenological control of the contralateral lung, the fluoroscope alone is inadequate because early fresh invasions escape fluoroscopic detection, even when roentgenologically present. Constant study of films is urged.

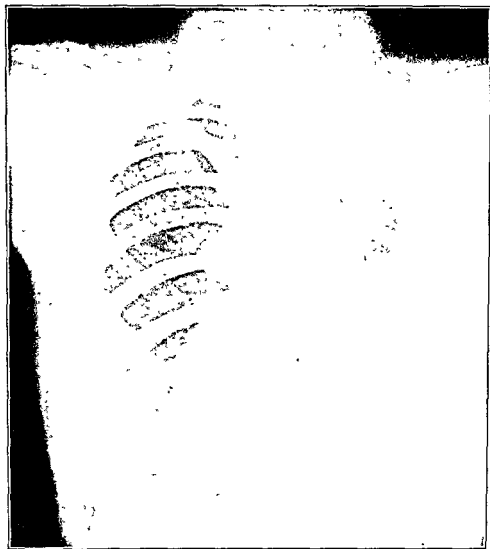


Fig. 18—Left lung fully expanded two years, following five years pneumothorax treatment because of a caseouspneumonic tuberculosis with cavity. Patient clinically well four years. Focus in apex of right lung unchanged in five years. Sputum negative for six years.

*Roentgen Films.*—While we must acknowledge the supreme advantage of roentgen films in supplying a permanent record, the examination of a single film must never be made with inordinate faith, and the last film should be minutely compared with the former ones. In the interpretation of the markings in the contralateral lung, one must differentiate between actual pathological

changes and changes due to circulatory stasis, which are especially marked in cases presenting a bulging mediastinum.

By permitting a slight reëxpansion of the collapsed lung, thus allowing the mediastinum to assume a more normal position, the shadows due to circulatory disturbance rapidly disappear.



Fig. 19.—Same case as Fig. 18. Six months later. Patient stricken with profuse hemoptysis. Focus in right apex progressive with small cavity formation. Sputum again positive.

Films taken at the height of deep inspiration expose most authentically any disease in the contralateral lung, but alterations in the position of the mediastinum are best seen in films taken at the end of expiration.

During the early phases of collapse therapy, films should be made after every third or fifth inflation if one resorts to small amounts of gas at short intervals: and later on (after the first two or three months), films should be



made at periods not exceeding a month. Ambulant cases are "filmed" at least once every three months throughout the complete course of their treatment.

As has been pointed out, in the selection of material and in control of treatment, one always has to contend with the transmission of auscultatory findings from the worse diseased lung to the opposite side. It may be exceedingly difficult

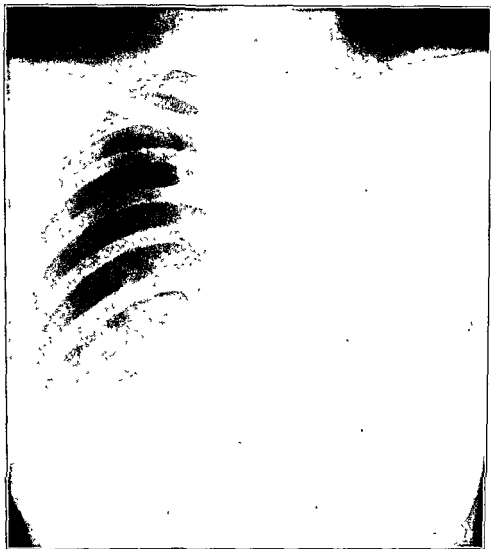


Fig 20—Same as Fig. 19. Three months later. Pneumothorax on right side. No cough nor expectoration. Sputum negative one month.

to differentiate these transmitted auscultatory phenomena from those due to actual disease, but an endeavor should be made to find out their source by localizing their point of maximum intensity and, in the case of transmitted phenomena, one will be led to the opposite lung. A decision will be additionally facilitated by a study of roentgen films, which will reveal an entire absence of disease in the contralateral lung that could account for the character of the auscultatory findings. The flexibility of the mediastinum will also have an important bearing on

adventitious sounds elicited in the contralateral lung, for occasionally râles, when present in the opposite lung before inflation, will change in character or disappear immediately afterward, in the presence of a flexible mediastinum.

**Analysis of Clinical Phenomena.**—In the presence of actual or threatened invasion of the opposite lung, one must exclude the contralateral lung as a source of unfavorable clinical signs or symptoms such as fever, increased expectoration or hemoptysis.

**Fever.**—Febrile reaction or ephemeral exacerbation within twenty-four hours after inflation with a satisfactory collapse, would point suspiciously to the opposite lung, especially in the absence of an exudate or of adhesions.

Recurrence of fever after an afebrile period occurs most commonly under the following conditions: appearance of exudate in the pneumothorax cavity, insufficient collapse, reëxpansion of the lung, progression or extension of disease in the contralateral lung, extrapulmonary tuberculous complications (especially enteritis), and acute nontuberculous respiratory infections. Exudate is ascertainable by fluoroscopy and, following aspiration, the fever usually abates.

Differentiation of fever is of utmost importance, but this will be found exceedingly problematical at times; it may be ascribed to progression or extension of disease in the contralateral lung, or to inadequate collapse, or reëxpansion of the lung, or to tuberculous or nontuberculous complications or intercurrent disease. In case the fever is due to reëxpansion, if inflation is not undertaken at once, progression in the collapsed lung will be furthered, or an early obliterative pneumothorax become established. Should the fever be attributed to progression or extension of disease in the contralateral lung, more collapse would only aggravate the disease already present. The contralateral lung must be thoroughly examined and the results critically compared with the records of all former examinations (films and physical).

Additional collapse is prohibited if evidence is found of fresh invasion or progression of disease in the opposite lung; on the other hand, if none of these signs are manifest, further collapse is not objectionable.

Fever due to extrapulmonary tuberculous complications is uninfluenced by inflation, and usually associated with localizing symptoms, which develop coincidentally with, or shortly after the febrile reaction. An elevation of temperature of this character may be due to an obscure tuberculous enteritis or ischiorectal abscess, with slight or complete lack of symptoms. The underlying motive for the fever may escape discovery unless purposely sought for, especially in the presence of contralateral lung disease, which must always be regarded with suspicion.

Fever due to acute infections, particularly those of the upper respiratory tract, tonsils, sinuses and teeth, may be confusing during the period of its onset and until the localizing symptoms appear.

A persistent fever (such as minor degrees of continuous low grade temperatures, 99° to 99.6° F.) in spite of obviously satisfactory collapse, is seen, now and then, in patients who are seemingly clinically well in other respects. Because of its diminutive quantity, detection is not effected for a time. But, this type of

fever is not always due to the tuberculous process itself: nontuberculous complications, such as chronic focal infections, thyrotoxicosis, etc., may be the basis.

There is, however, this medium for discrimination: that when the fever is due to tuberculosis, it is more responsive to rest and more aggravated by exercise. Clinical, physical diagnostic or roentgenological evidence will usually determine the rôle of the contralateral lung.

Another type of continuous fever encountered is that in which treatment has been accompanied by a reduction of temperature amounting to two or more degrees, but there still remains an average daily maximum of 100.6° F. in spite of a satisfactory collapse. When temperature of this character is due solely to contralateral lung disease, auscultation alone will usually supply ample evidence of its origin.

*Influence of Contralateral Lung Disease on Sputum.*—It is of equal importance to eliminate the contralateral lung as a source of tuberculous sputum; when undeviating, with an essentially negative contralateral lung and an apparently satisfactory collapse, this indication betokens that diseased tissue is not sufficiently collapsed, either because of the presence of adhesions, particularly apical and those in the costovertebral gutter which are not always revealed by the usual anteroposterior roentgen films, or because of the existence of rigid-wall excavations. Not infrequently lateral films will reveal the source of the sputum. However, when the contralateral lung is diseased, and a satisfactory collapse of the worse diseased side has, to all appearance, been achieved, the persistence of bacilli-containing sputum in quantities of 20 or 26 c.c. daily, should lead one to deeply suspect its origin to be in the contralateral lung. The demonstration of moisture upon auscultation will provide added substantiation of this misgiving.

Under these circumstances, one will be obliged to decide whether to allow moderate reëxpansion, thus relieving the contralateral lung, or to further collapse the worse diseased lung or institute a bilateral pneumothorax. In this event, the twenty-four-hour quantity of sputum must be measured carefully each day, and its relationship to inflation and physical findings in each lung closely observed.

In the presence of contralateral lung disease, inflations are sometimes followed by a sudden increase in temperature, which, when associated with an increase in sputum amount, points more strongly to the contralateral lung as the source.

If responsibility for the greater abundance of expectoration is traceable to the contralateral lung, the physical examination will usually reveal a heightened amount and distribution of râles.

Stereoscopic films, when carefully compared with all prior films, should determine if the contralateral lung is responsible for the sputum increase. Other evidence of disease progression may be noted.

The influence of the patient's bed posture during coughing paroxysms and lung drainage should be watched with care; in so doing, considerable evidence may be obtained that may tend to show the side from which the sputum emanates, as some positions will afford freedom from cough and expectoration due

to retention of secretion in dependent portions of the lung, whereas, other positions will provoke coughing paroxysms with abundant expectoration, due to free drainage.

A final decision can best be attained only after a correlation of all findings.

**Hemoptysis.**—Severe hemoptysis sometimes takes place in the course of pneumothorax treatment, and always directs attention to the contralateral lung,—more so if it is diseased.

Although it is not easy to determine from which side bleeding is occurring, a confident verification of this point must be arrived at; for, if the bleeding is proceeding from the collapsed lung, further collapse is demanded; but if from the opposite lung, further collapse is strongly contraindicated and a bilateral pneumothorax must be considered. It is possible to acquire much enlightenment from the patient's own statements regarding certain subjective phenomena immediately before, or very early during the hemoptysis. These sensations are commonly described as a feeling of tightness, constriction, pain, "rattling," or "fluttering," the exact location of which the patient will indicate. While misleading at times, the information is undeniably of material benefit.

As a result of bleeding, aspiration of blood into dependent portions of the lung is unpreventable; it is always more extensive on the bleeding side. The presence of this blood will furnish râles which are quite characteristic, and may be readily heard in portions of the lung into which blood has been aspirated. These râles have been variously described as "medium" or "small bubbling" or "crackles." At first they are nonresonating, only becoming resonating later on with the development of consolidation.

In the presence of uncontrolled bleeding from the contralateral lung, one must consider a bilateral pneumothorax.

**Comparative Significance of the Various Types of Contralateral Lung Lesions Based Upon End-Results.**—In the selection of material and in determining the indications for collapse, an accessory of decided value will be found in a comparison of end-results in the various types of contralateral lesions; in this way, one will be able to judge the prognostic significance of disease in the contralateral lung, with collapse of the worse diseased side.

By a study of the table of end-results (Table III) for the purpose of determining the significance of contralateral lung lesions, it will be seen that only 97, or 23 per cent of the cases included in this series, presented an essentially negative contralateral lung.

The "no free pleural space" cases have been included in this series as controls, since their treatment was identical, with the exception that no pneumothorax was established. They also emphasize that satisfactory end-results are as much dependent upon the presence of free pleural space and the character of collapse attained, as they are upon the presence or absence of disease in the opposite lung.

In comparing the deep peribronchial infiltration with the essentially negative contralateral lung, it will be noted that in the presence of a satisfactory collapse, 7 per cent. less are clinically well and 6 per cent. more are dead in the former than in the latter group.

From a prognostic standpoint, disseminated bronchogenic caseous extension in the opposite lung is very serious, because, when compared with the essentially negative contralateral lung group, it will be seen that 26 per cent. less are clinically well and 19 per cent. more are dead in the former than in the latter group.

In comparing the group of active fibrocaseous infiltration of the contralateral lung with the essentially negative opposite lung, it is evident that only 4 per cent. fewer cases are clinically well, but 8 per cent. more are dead.

In comparing the active with the quiescent fibrocaseous infiltrations, it will be seen that 2 per cent. more are clinically well, 2 per cent. more are arrested and 2 per cent. less are dead in the quiescent than in the active fibrocaseous group.

This difference in end-results is not as great as one would expect, but it is probable that activity undoubtedly existed in some cases which we were obliged to classify as quiescent because they could not be demonstrated as active. However, these figures are entirely consistent when one compares the end-results (Table III) in both the active and quiescent fibrocaseous opposite lung lesions, with the essentially negative contralateral lung.

As previously stated, the disseminated bronchogenic caseous extensions, occupying the perihilar and lower portions of the lung, offer a much more unfavorable outlook than the fibrocaseous lesions which usually occupy the upper portions of the lung.

Our observations convince us that the disseminated bronchogenic caseous extensions are the most serious type of contralateral lung lesions with which we have had to deal.

From a study of the above statistics, as regards the percentage clinically well and dead in the presence of a satisfactory collapse, some may be of the opinion that results equally satisfactory are attained by the usual sanatorium regimen without pneumothorax.

Nevertheless, the value of pneumothorax therapy in this series will be clearly shown by a comparison of end-results in cases satisfactorily collapsed with those having "no free pleural space," which serve as controls.

It will be observed that in this series (Table III), a patient's chances for recovery were much better with any type of contralateral lung disease in the presence of a satisfactory collapse than in the case of the patient who had an essentially negative lung, in which collapse was not possible because no free pleural space could be found.

**Observations on Progression and Extension of Disease in the Contralateral Lung.**—The term "progression of disease" refers to those cases in which there was exacerbation of disease in a contralateral lung already diseased, whereas, the term "extension of disease" refers to those in which invasion of an essentially negative contralateral lung took place.

Only those instances of progression or extension of disease in the contralateral lung occurring during the actual period of pneumothorax treatment are included in our figures.

We have omitted the cases where progression and extension of disease took place in the terminal phases after pneumothorax treatment was abandoned

because the development of these complications was not associated with, or related to the period of collapse therapy.

Minor degrees of progression and extension of disease of a character which escaped physical diagnostic or roentgenological methods of recognition may have occurred.

Many cases experienced alternating periods of exacerbation and quiescence of activity of contralateral lung disease while under collapse, but the periods of exacerbation were temporary and did not demand discontinuance of collapse therapy.

Changes of this nature are not infrequent throughout the course of any tuberculous process and may or may not have been related to collapse therapy.

When progression of disease in the opposite lung is of mild nature, a prolongation of intervals and the introduction of small amounts of gas are necessary, thus permitting of some reexpansion of the collapsed lung, which will frequently bring about a decrease of activity in the contralateral lung and a coincident improvement.

Severe and rapid progression of disease in the contralateral lung demands temporary cessation of pneumothorax treatment. One will be confronted with a complicated problem in deciding upon future procedure, and the behavior of both lungs during this brief period of observation will render a conclusion possible.

When reexpansion of the collapsed lung is not followed by improvement of disease on the opposite side, one will be justified in considering the feasibility of bilateral collapse. If this procedure is adopted, the primarily collapsed lung should be permitted to reexpand as much as possible without evidence of reactivation of disease in it, and at the same time it must still be under control, so that recollapse can be instituted as indications require. If no reactivation occurs, one can proceed cautiously with the contralateral lung collapse. The inflations are then made alternately, the intervals and amounts of gas being determined by the indications and contraindications in each lung. We have carried out bilateral collapse in 20 cases, eight of which are clinically well and twelve dead. The prognosis in cases so severe as to demand a bilateral pneumothorax is very grave, but the procedure will often add much comfort and prolongation of life to the patient.

Out of the 423 cases included in this study, 345 cases were collapsed. Of the 345 collapsed cases, 264 had demonstrable disease in the opposite lung, 82 cases had well-defined peribronchial infiltration, but in 182 cases the disease amounted to fibrocaseous infiltrations or disseminated bronchogenic caseous extension. In these 264 cases progression of disease in the contralateral lung took place in 24 cases as shown in Table IV.

**Influence of Partial Collapse on Contralateral Lung.**—Inferences drawn from a statistical analysis of the behavior of the contralateral lung in the presence of a partial collapse of the worse diseased side are unreliable for the reason that the more the partial collapse partakes of the character of a satisfactory collapse, the more the end-result will approach those of a satisfactory one and, contrariwise, the more limited or localized the partial collapse, the more the

TABLE IV  
PROGRESSION OF DISEASE IN THE CONTRALATERAL LUNG IN COLLAPSED CASES.

Status of Contralateral Lung	Number of Cases	Progression Number Cases	Character of Collapse
Deep peribronchial infiltrations	82	2	2 partial
Disseminated bronchogenic caseous extensions	36	3	1 satisfactory 2 partial
Active fibrocaceous infiltrations	109	17	7 satisfactory 10 partial
Quiescent fibrocaceous infiltrations	37	2	2 partial

end-result will approach those of the "no-free-space" cases. Furthermore, the end-results in pneumothorax therapy in cases under partial collapse are, for the most part, but slightly influenced by the behavior of the contralateral lung and are largely dependent upon the type of disease in the worse diseased lung and the character of collapse.

There can be no constant uniformity in end-results in cases under partial collapse, for the reason that there is no regularity in the character of partial collapse.

Even with these facts in mind, reference to Table II will reveal certain illogical discrepancies in the partial-pneumothorax group which might lead to erroneous conclusions unless one is familiar with the circumstances surrounding these cases. For example, in the "deep peribronchial infiltration" group under partial collapse, there were 33 cases, 60 per cent, of which are dead; whereas, of 21 "no free pleural space" cases, with the same type of contralateral lung, only 43 per cent. are dead, which fact would lend support to the opinion that in the "deep peribronchial" cases, the partial pneumothorax was not only of no value, but was actually detrimental. An investigation of the individual case records of this group shows that the partial collapse was of value, for 16 were temporarily improved and only 4 were progressively fatal, whereas all the "no free pleural space" control cases were progressively fatal.

Furthermore, even though these 16 improved cases were ultimately fatal, they should not be altogether chargeable to partial-pneumothorax failures, since 3 cases died of intercurrent disease unrelated to tuberculosis. Six more patients in this group voluntarily discontinued treatment, believing themselves cured, and later suffered a relapse of their disease which proved fatal.

As further evidence of the favorable influence of a partial pneumothorax in this group of cases, 32 out of 33 cases under partial compression had a tubercle-bacillus-positive smear before pneumothorax treatment and only 14 had a positive smear on discontinuation of pneumothorax treatment, whereas of the 20 "no free pleural space" cases, 19 had a positive smear before sanatorium treatment and 14 had a positive smear upon discontinuation of treatment.

Out of 81 cases with an essentially negative contralateral lung, extension was noted in 4 instances, 3 of which were satisfactory collapses and the extension was such that it required discontinuation of pneumothorax treatment.

## INFLUENCE OF ARTIFICIAL PNEUMOTHORAX ON SYMPTOMS.

After the first few inflations, there may be some increase in cough and expectoration as sputum is forced from the lung. If adhesions are present, the patient often feels a sensation of tugging, or actual pain; when the lung is adhesion-free, in a favorable case, he soon adjusts himself to the injections of gas; the temperature lessens, cough and expectoration decrease or cease altogether and the patient begins to feel stronger and better. As the tuberculo-toxemia is overcome, the appetite improves and weight is gained.

Determining the influence of artificial pneumothorax upon symptoms while patients are undergoing the usual sanatorium regimen is not done without some difficulty, as it is always debatable which method has been of greatest value. To further comparison more readily, we have included in our studies cases selected for pneumothorax therapy where no gas could be introduced because of absence of free pleural space. These cases are included for comparison because (aside from collapse therapy) their treatment was the same as that of the pneumothorax cases, with the exception of them not being under observation as long as the satisfactory collapse cases; but they were under observation for a longer period than those wherein adhesions prevented a satisfactory collapse of the lung, and are referred to by us as "partial collapse" cases.

We have carefully studied 600 cases regarding the influence of pneumothorax on fever, weight and sputum. In this series of 600 cases, there were 281 cases belonging to the National Tuberculosis Association classification, Stage III C. A satisfactory collapse was established in 29 per cent. of these, a partial collapse obtained in 50 per cent., and in 21 per cent. no free pleural space was found.

A summary of our observations follows:

**Fever.**—Of 235 cases comprising a satisfactory collapse group, 203, or 86 per cent., were febrile before pneumothorax treatment; and 152, or 77 per cent., became afebrile. Among 245 partial collapse cases, 224, or 91 per cent., were febrile before treatment; and 78, or 34 per cent., became afebrile. In the no-free-space group, comprising 120 cases, 110 (91 per cent.) were febrile before pneumothorax was attempted; and 34, or 30 per cent., became afebrile as a result of sanatorium régime.

**Sputum.**—Of 235 satisfactory collapse cases, 176, or 70 per cent., had a positive sputum before pneumothorax treatment; and 123, or 70 per cent., became negative after treatment. Of 245 partial collapse cases, 227, or 90 per cent., had a positive sputum before treatment; and 57, or 25 per cent., became negative. Of 120 no-free-space cases, 111, or 92 per cent., had a positive sputum when pneumothorax treatment was attempted; and 17, or 15 per cent., became negative as a result of sanatorium treatment.

Of 600 cases comprising this analysis, 514 had a positive sputum and 218 became negative by concentration methods of examination (author's modification of the Ellermann and Erlandsen method<sup>14</sup>). Of the 218 which became negative, 147, or 69 per cent., were satisfactory collapses; 54, or approximately 25 per cent., were partial collapses; and 17, or approximately 8 per cent., were no-free-space cases.



**Weight.**—Among the 235 satisfactory collapse cases, 65 per cent. had lost weight before treatment, 7 per cent. lost weight during pneumothorax treatment and 87 per cent. gained weight during pneumothorax treatment. Of 245 partial collapse cases, 69 per cent. had lost weight before treatment, 11 per cent. lost weight during pneumothorax treatment and 73 per cent. gained weight during and after pneumothorax treatment. Among the 120 no-free-space cases, 80 per cent. had lost weight before sanatorium treatment, 18 per cent. lost weight during sanatorium treatment and 69 per cent. gained weight during and after sanatorium treatment.

These data, at the first glance, suggest that the results of treatment in the satisfactory collapse cases were better than in the partial collapse or no-free-space cases, because the satisfactory collapse cases were earlier ones, the partial collapse more advanced, and the no-free-space cases the most advanced. However, this is not so, although the clinical groups in Table I (except clinical groups 5 and 6) are arranged somewhat according to their prognosis, the most favorable being clinical group 1, and the most hopeless, clinical group 8. The impression that the satisfactory collapse cases were earlier cases and the no-free-space cases were more advanced finds no support when one notes that satisfactory collapses were proportionately no greater in clinical groups 2 and 3 than partial collapses, and even in the acute infiltrating types (clinical group 4, Table I) there were many more satisfactory collapse cases than no-free-space cases. Also, in the bilateral fibrocaseous cavernous group (none of which could possibly be considered earlier types) the number of satisfactory collapse cases fairly well approached the no-free-space cases; yet, a comparison of the clinically well and those who are dead furnished abundant evidence that recovery did not take place because a case was of a more favorable type, but (all other factors being equal) because a satisfactory collapse or even a partial collapse gives a case in any clinical group a better chance for recovery or arrest of disease than no pneumothorax at all.

Of 235 satisfactory collapse cases in our series, 86 per cent. were febrile before treatment. In 18 per cent., fever had been present six months or more, and in 30 per cent. its daily average was 101° F. or over. Of the 245 partial collapse cases, 91 per cent. were febrile before treatment, while in 25 per cent., fever had been present six months or more and in 43 per cent. its daily average was 101° F. or more. The 120 no-free-space cases also were 91 per cent. febrile before pneumothorax was attempted, and in 28 per cent. the fever had existed six months or more; however, 38 per cent. had a daily average of 101° F. or more. Therefore, the percentage in the partial collapse and no-free-space cases was the same, but the duration of fever was somewhat longer (3 per cent.) in the no-free-space cases, while its daily average maximum was higher in the partial collapse cases (5 per cent.).

Regarding loss of weight,—65 per cent. of the satisfactory collapse cases had lost weight before treatment, while 69 per cent. of the partial collapse cases and 80 per cent. of the no-free-space cases had lost weight prior to treatment. But, in the satisfactory collapse cases, 12 per cent. had lost over 20 pounds, and 21 per cent. had lost over 20 pounds in each of the partial collapse and

no-free-space cases. Relatively, then, the loss was greater in the partial collapse cases.

The sputum findings, as to tubercle-bacilli content, according to the character of the pneumothorax, were as follows:

In the satisfactory collapse cases, 75 per cent. were positive before treatment and 25 per cent. had a daily average of 20 c.c. or more. In the partial collapse group, 92 per cent. were positive before treatment and 40 per cent. had a daily average of 20 c.c. or more; in the no-free-space cases, 91 per cent. were positive before pneumothorax treatment was attempted and 39 per cent. had a daily average of 20 c.c. or more.

Among our 600 cases, 284 had serious tuberculous complications before treatment, such as laryngitis, enteritis and severe hemoptysis.

Serious tuberculous complications were present in 43 per cent. of all the satisfactory collapse cases, but the partial collapse cases had serious tuberculous complications in 52 per cent. of all cases and the no-free-space cases had serious tuberculous complications in 45 per cent. It seems probable that the value of a partial collapse may lie, not so much in the actual lung collapse which often is slight and transient, as in the secondary pleuritic thickening with adhesion formation, which takes place following the obliterative changes incident to gas introduction and serves to maintain the lung at partial rest.

**End-results of Treatment.**—Large statistics dealing with the end-results of artificial pneumothorax in the treatment of pulmonary tuberculosis show singular compatibility. Naveau's<sup>15</sup> comprehensive study of Rist's large material, comprising 1195 cases subjected to artificial pneumothorax between 1911 and 1922, show results nearly identical with those we obtained in 600 cases of corresponding types of disease subjected to artificial pneumothorax during the same twelve-year period, from 1911 to 1922.<sup>16</sup>

Of 570 cases of fibrocaceous tuberculosis in Rist's series, the results were: 31 per cent. clinically cured, 17.5 per cent. improved, 17.5 per cent. stationary and 34 per cent. unimproved and dead. Our own results in 423 cases of fibrocaceous and fibrocaceous cavernous tuberculosis were: 32 per cent. clinically cured, 20 per cent. arrested, 16 per cent. unimproved and 32 per cent. dead.

Burnard,<sup>17</sup> although using a different classification of end-results than our own, also reported results similar to the above in 237 cases treated from 1912 to 1922, of which 42 per cent. are able to work, among whom 26 per cent. are clinically well.

Saugman's<sup>18</sup> statistics, covering a fourteen-year period ending in 1921, during which time he treated 500 cases, showed 40 per cent. able to work. Also Brauer and Spengler<sup>19</sup> reported 31.8 per cent. healing after fifteen years' observation, and Maendl,<sup>20</sup> upon a basis of a questionnaire sent to 180 sanatorium and tuberculosis specialists, totalling 1330 cases under treatment from two to twelve years, found permanent results (*Dauererfolge*) in 66 per cent.

When one takes into consideration that nearly all reports deal mostly with severe cases of pulmonary tuberculosis treated by artificial pneumothorax after the failure of other methods, it must be admitted that artificial pneumothorax

has not only become an accepted method of treatment, but an obligatory one in certain cases.

Drawing conclusions from a study of any large series of cases that covers a long period of years is handicapped by the difficulty of accumulating accurate information regarding the present status of many cases. We were prompted by the notorious unreliability of statistics to reduce to a minimum any error in data, which at the very beginning of our work led us to accumulate information regarding all patients subjected to pneumothorax treatment.

Because of the fact that most cases included in our series were not of the migratory consumptive class, but permanent residents of the Pacific Northwest, our effort has been greatly facilitated.

Pneumothorax cases are never discharged from observation. In accordance with this policy, we have maintained contact with most of our living cases by periodic reexamination and, when this was impossible, by correspondence. Many cases completed ten years ago still submit themselves to an annual or biannual reexamination.

In order to complete our records, we sent questionnaires to all patients in this series concerning whom there was doubt regarding their present status and when no replies were received, their condition was classified according to their last report, but none of them were given a better rating than *favorably influenced*, irrespective of how much the last report warranted a higher one. Cases in which the period of treatment or observation was so brief that reliable conclusions were impossible, were excluded. No case has been classified *clinically well* (*apparently cured*) until three years had elapsed after the lung expanded and the patient was living under ordinary conditions of life. Regardless of how apparently clinically well in less time after the lung had expanded, they have been recorded as *arrested*. No case has been considered *clinically well* (*apparently cured*) unless it more than conformed to the requirements of the National Tuberculosis Association.

In our final analysis we again reviewed in detail all records pertaining to each case, including the reexamination of thousands of roentgen films and orthodiagrams. We feel, therefore, that these statistics are as accurate as it is possible to present them.

**Control of Pneumothorax Cases.**—Realizing the great importance of sanatorium education and observation, we have not accepted any patient for pneumothorax treatment who was unwilling to submit to an initial period of sanatorium care. All patients received their early pneumothorax treatment in the Portland Open Air Sanatorium. They were not subjected to artificial pneumothorax treatment until after a reasonable trial of the usual sanatorium methods, unless they were of a character that justified the assumption that a cure would not be effected by the usual treatment. Quite naturally, some were subjected to pneumothorax who may have recovered without it. However, our conservatism in selecting patients for artificial pneumothorax is attested by the fact that there were only 5 per cent. of recoveries and 65 per cent. of deaths in cases in which pleuritic adhesions prevented pneumothorax treatment, whereas in cases in which

a satisfactory collapse was accomplished, 48 per cent. are clinically well and 22 per cent. are dead.

*The Period of Sanatorium Treatment.*—This was reduced to the minimum compatible with safety, patients being discharged to ambulant care as soon as possible.

Before patients were permitted to receive ambulatory treatment they remained in the sanatorium until, under a system of regulated activities, we were convinced that they could report for reinflations without untoward results.

Ambulant treatment and observation in every case was carried on as long as possible, at times under the most unfavorable circumstances, as many patients were obliged to journey from remote points in the Pacific Northwest for reinflation. In addition, the vast majority of cases were compelled to resume occupational activities early, because of limited circumstances. However, it is not always necessary that patients be forbidden all occupational activities while under pneumothorax treatment. As a matter of fact, nearly all of our pneumothorax patients who are being treated while ambulant, are engaged in some sort of gainful occupation. Nevertheless, patients are advised against work involving physical strain. The extensive activities a patient can engage in at times without apparent harm are striking to observe. I have in mind a Columbia River fisherman who was under pneumothorax therapy five and a half years, and during the last four and a half years of his pneumothorax treatment he performed full field duty at his work, and is clinically well today.

*Duration of Pneumothorax Treatment and Observation.*—It has been our policy to maintain a pneumothorax for at least three years after the disappearance of all constitutional disturbances including tubercle bacilli in the sputum in cases having limited lesions of rather short duration and in good general condition and when rapid response to treatment took place. However, in those cases who had had a stormy career with extensive disease of long duration before pneumothorax treatment was instituted, we have felt it wise to continue pneumothorax treatment as long as possible and, while the most favorable results are associated with a satisfactory collapse over a prolonged period, we have seen good results in cases in which the period of treatment was relatively short.

Aside from the pneumothorax, the "no-free-pleural-space" cases were assigned the same treatment as the collapsed cases,—hence, they serve as splendid controls and are included in Table III.

*Classification of Pneumothorax Character.*—The end-results of pneumothorax therapy are so intimately associated with the character of the pneumothorax that our statistics were tabulated accordingly. Our classification of the nature of the pneumothorax is as follows:

*Satisfactory Collapse.*—This denotes that a sufficient degree of collapse or compression of diseased lung tissue was produced, which (in conformity with our experience), if maintained, would exclude the diseased lung as a source of any symptom. We refer particularly to such symptoms as persistence of germ-laden sputum in quantities amounting to 20 or 30 c.c. or more daily, fever of 100° F. or more, and tuberculotoxemia extending over a period of two or three months after beginning pneumothorax treatment.

In former publications, we have used the term *satisfactory compression* in the same sense as we now use *satisfactory collapse*. Although satisfactory compression was used in a clinical sense and not an anatomical one, we prefer the term *satisfactory collapse*. From the beginning of our work, we have maintained the minimum degree of collapse or compression necessary to accomplish satisfactory clinical results. In most cases, this amounted to a *pneumothorax of rest*, but in some instances actual compression of lung tissue was necessary to secure desired results. Nevertheless, if satisfactory results were obtained, the pneumothorax was classified as a satisfactory collapse.

*Partial Collapse.*—This term means that a satisfactory collapse or compression was unattainable, adhesions being our greatest obstacle. Thus, even

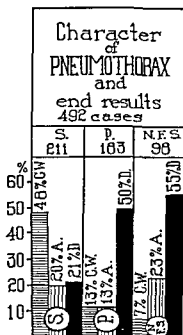


Fig. 21.—C-W, clinically well. A, arrested. D, dead. S, satisfactory collapse. P, partial collapse. N-F-S, no free space.

though an almost total collapse or compression of the lung was produced, if we were unable thereby to establish a satisfactory pneumothorax or to close cavities because of adhesions, the case was placed in the partial collapse group for the obvious reason that the character of the pneumothorax was not satisfactory.

*No-Free-Space.*—No explanation is necessary regarding this term, except that no case has been placed in this class until repeated attempts over all lobes of the lung verified the absence of free pleural space.

*Importance of a Good Collapse.*—The influence of the character of the pneumothorax on end-results and the importance of a satisfactory collapse are shown in Fig. 21. Of the 492 cases included in this study 211 (43 per cent.) had a satisfactory collapse, and 48 per cent. are clinically well, 20 per cent. arrested, and 21 per cent. dead. Of 183 (37 per cent.) partial collapse cases, 13 per cent. are clinically well, 13 per cent. are arrested and 50 per cent. are

dead; while of 98 (20 per cent.) no free-space cases, only 7 per cent. are clinically well, 23 per cent. are arrested, and 55 per cent. are dead. The value of a satisfactory collapse is even more strikingly demonstrated in Fig. 22. Of the 133 cases who are clinically well, 76 per cent. had a satisfactory collapse, 18 per cent. had a partial collapse and 5 per cent. were no-free-space cases, recovery having taken place as result of sanatorium treatment. On the other hand, of the 193 dead, 23 per cent. were satisfactory collapse cases, 47 per cent. were partial collapse cases and 30 per cent. were no-free-space cases. The

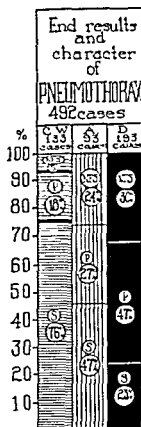


Fig. 22—C—W, clinically well. A, arrested. D, dead. S, satisfactory collapse. P, partial collapse. NS, no free space.

higher percentage of deaths in the partial collapse group, as compared with the no-free-space group, is due to the large number of deaths (13) among the partial collapse cases (17) in the acute forms of phthisis, also to the large number of deaths among the 12 partial collapse cases in the bilateral group, in which 7 deaths occurred. A partial collapse, notwithstanding, is of unquestionable value, as shown by Fig. 21

At the same time, we are quite satisfied that in most cases a partial pneumothorax should be abandoned and other operative collapse procedures substituted. This would give a 40 or 50 per cent. chance of recovery, instead of less than

a 20 per cent. one, which is the best result one can expect from a partial pneumothorax. However, if other surgical collapse procedures cannot be carried out, a partial collapse is better than none at all.

The end-results of pneumothorax treatment are tremendously influenced by many factors: *First*—those which have to do with the disease itself, such as

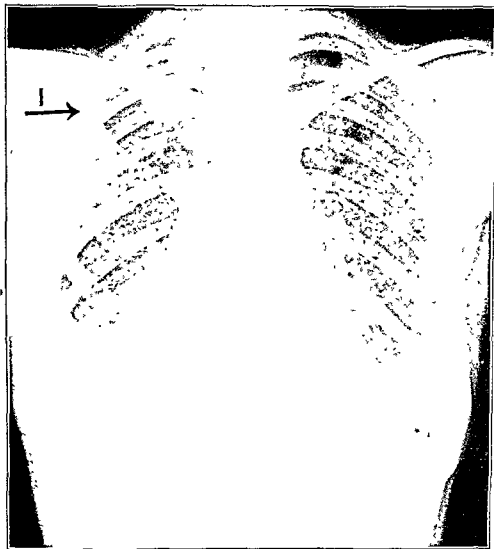


Fig. 23.—Caseouspneumonic tuberculosis of right lung with multiple cavities and metastatic extension to left lung. Patient ill one year. Temperature 100°–101° F. Weight 101 pounds. Sputum 40 c.c. positive.

its character, extent, degree of activity, presence of complications and status of the contralateral lung. *Second*: the character of the pneumothorax, that is, whether an efficient collapse is obtained or not. *Third*: complications which arise during treatment and actuated by it and those independent of treatment. *Fourth*: social and economic conditions which influence the length of treatment. However, if environmental and social conditions affecting the patient are favor-

able, and the patient gives loyal coöperation, and no contraindications for pneumothorax in the way of complications are present, the end-result, according to our experience, depends, *first* (and foremost) upon the type of disease, *second*, upon the character of the pneumothorax, and *third* (and least important), upon the condition of the opposite lung (Figs. 23, 24, 25, 26).

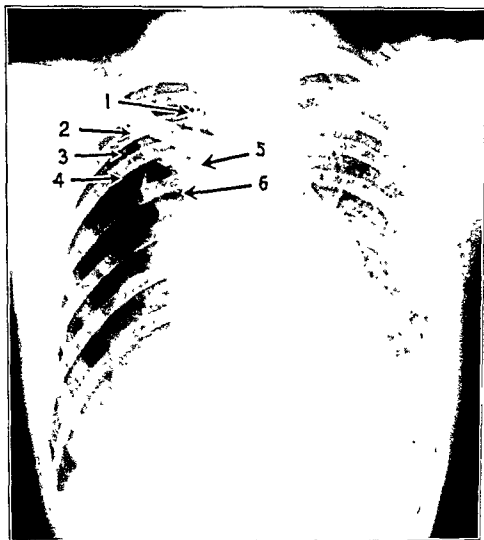


Fig. 24—Same case as Fig. 23. Three months later under pneumothorax treatment. Adhesions at 1, 2, 3, 4 preventing closure of cavities 5 and 6. Sputum unchanged. Temperature 100° F. General condition essentially the same.

While our entire material now comprises over 1700 cases of pulmonary tuberculosis subjected to artificial pneumothorax since January 1, 1911, we can best illustrate the value of treatment by presenting the end-results obtained in 492 cases, representing forms of pulmonary tuberculosis in which pneumothorax treatment was admittedly indicated and therefore cases likely to be selected for treatment. We excluded all cases treated within two years preceding our study.



also all cases under treatment at the time, so as to give results of a more or less permanent character. Furthermore, no case was classified clinically well unless the sputum was continuously negative, with an absence of all signs of activity, for a period of two years. Cases in which the above conditions had existed for three consecutive months were classified as arrested. No case in the series was



Fig. 25—Same case as Fig. 24 Two months later after the adhesion had been severed. One cavity still uncollapsed. The opaque shadow above the right hemidiaphragm is skiagenol introduced to study configuration of an adhesion in the costovertebral gutter. Temperature 99°—100° F. Sputum 15 c.c. T. B. Positive. Weight 105 pounds.

subjected to pneumothorax until after a reasonable trial of sanatorium care, unless the case was of a character which justified the assumption that a cure would not be accomplished by such treatment. Of the 492 cases, 65 were moderately advanced and 347 were far advanced (National Tuberculosis Association Classification). No case of incipient tuberculosis was treated.

For the purpose of showing the comparative value of artificial pneumothorax in different forms of pulmonary tuberculosis, and also to show the value of a satisfactory collapse of the lung, as compared with only a partial one where adhesions prevented closure of cavities, we arranged our cases in five clinico-pathological groups, and tabulated the results accordingly (Fig. 27). The cases



Fig 26—Same as Fig 25, four years later. Pneumothorax treatment was continued three years. Right lung fully expanded in six months. Left lung clear. Temperature normal. No sputum. Weight 162 pounds.

wherein adhesions prevented any gas introduction were included for comparison, because they received the usual sanatorium care.

**CLINICAL GROUP I**—This group comprised 194 cases of exudative, productive tuberculosis, progressive in character, with little or no cavitation. Sixty-five were moderately advanced (Stage II), and 129 were far advanced (Stage III). Of the 194 cases, we were able to establish a satisfactory collapse in 99,

53 per cent. are clinically well, 15 per cent. are arrested and 21 per cent. are dead. The remaining cases were either favorably influenced, temporarily improved or unimproved. But, if we should exclude five cases from the above group where death was due to extraneous causes not related to tuberculosis, such as

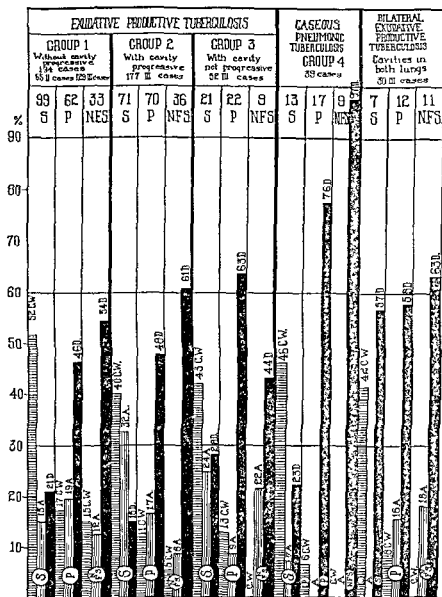


Fig. 27.—C-IV, clinically well, A, arrested D, dead S, satisfactory collapse P, partial collapse. N-F-S, no free space

accidental death, typhoid fever, etc., the clinically well would be 55 per cent. and the dead 17 per cent.

The results would appear still better if we excluded the fatal cases occurring among patients who discharged themselves voluntarily from treatment, believing themselves well, or were persuaded by well-meaning friends that no further

treatment was necessary. All of these patients were in good general condition at the time of leaving off treatment. Unfortunately, with the more favorable types of cases experiencing rapid improvement from pneumothorax treatment, the seriousness of the illness is soon forgotten. Treatment becomes boring and many failures will take place, because of discontinuation of treatment. For this reason the deaths in the satisfactory collapse cases in Clinical Group I are higher than in Clinical Group II, which were even more advanced cases.

In 62 cases in Clinical Group I, a satisfactory collapse could not be established because of adhesions. Of these partial collapse cases 17 per cent. are clinically well, 19 per cent. are arrested and 46 per cent. are dead.

In 33 cases, the free pleural space was obliterated by adhesions and no gas could be introduced; of these, 15 per cent. are clinically well, 12 per cent. are arrested and 54 per cent. are dead.

Among the 161 cases receiving pneumothorax treatment in Clinical Group I, 111 had demonstrable tuberculosis in the contralateral lung and in 54 it was active. And while progression of the disease took place in 12, only 7 compelled discontinuation of the pneumothorax.

In 2 instances a tuberculous process extended from the pneumothorax side to the opposite lung which had been considered free of disease. Neither case required cessation of the pneumothorax.

The largest proportion of satisfactory collapse cases, and likewise the best results in our entire series, were obtained in Clinical Group I. This suggests that pneumothorax treatment should be utilized in the treatment of chronic plithisis, before the disease has progressed to the formation of cavities and at a time when adhesions are less likely to prevent a satisfactory collapse. That pneumothorax treatment is justified in these earlier types of cases comprising Clinical Group I, is shown by the comparative results in the satisfactory collapse cases, partial collapse cases and those cases wherein no gas could be introduced.

**CLINICAL GROUP II**—This group comprised 177 cases of exudative, productive tuberculosis of a more advanced character than the preceding group; all had demonstrable cavities and all were far advanced (Stage III).

In 71 cases a satisfactory collapse was established and 40 per cent. are clinically well, 32 per cent. are arrested and 15 per cent. are dead. In 70 cases a partial collapse was established and 11 per cent. are clinically well, 17 per cent. are arrested and 48 per cent. are dead. And of 36 no-free-space cases 5 per cent. are clinically well, 8 per cent. are arrested and 61 per cent. are dead.

There were 141 cases under actual pneumothorax treatment in Clinical Group II, and of these, 119 had demonstrable tuberculosis in the contralateral lung, and in 70 it was active. Progression of disease in the contralateral lung took place in 12, and extension of disease from the pneumothorax side to the opposite previously healthy lung took place twice. Of the above 14 cases, the pneumothorax was discontinued in 9 because of the unfavorable course of the disease in the contralateral lung.

A satisfactory collapse was less frequent in Clinical Group II than in the preceding clinical group because of adhesions, and this, together with the more destructive nature of the disease, is manifested in the end results. This again

emphasizes the advisability of utilizing pneumothorax treatment earlier in the evolution of phthisis.

**CLINICAL GROUP III.**—This group comprised 52 cases of exudative, productive tuberculosis, all far advanced (Stage III), in which the caseation and softening phases of the disease had been passed through, leaving enormous cavitation with marked fibrosis. These cases were more or less stationary, at least only slowly progressive. Of the 52 cases in this group, a satisfactory collapse was established in 21, and 43 per cent. are clinically well, 24 per cent. are arrested and 28 per cent. are dead. A partial collapse was established in 22, and 13 per cent. are clinically well; 9 per cent. are arrested and 63 per cent. are dead. In 9 cases, no gas could be introduced and none are clinically well; 22 per cent. are arrested and 44 per cent. are dead. Of the 43 cases in Clinical Group III, under pneumothorax treatment, 34 had demonstrable tuberculosis in the contralateral lung, and in 21 it was active, becoming progressive in only three instances, when discontinuation of the pneumothorax was compelled.

A satisfactory collapse was no more frequent in this group than in Clinical Group II, but the results, as a whole, were somewhat better. However, instead of dealing with a more progressive type of phthisis, as in Clinical Group II, Group III comprised cases following a lingering course, with torpid lesions. Nearly all these cases were chronic invalids who had tried various climates and sanatoriums without success. All expectorated large quantities of sputum laden with tubercle bacilli, and all were potential sources of infection. Therefore, from the standpoint of prophylaxis alone, it is a splendid achievement to have restored some of these cases to health.

**CLINICAL GROUP IV.**—This group comprised 39 cases of caseous pneumonic tuberculosis; all were rapidly advancing types of disease, characterized by extensive invasion and associated with a violent symptom complex. Of the 39 cases in Clinical Group IV, 13 had a satisfactory collapse and 46 per cent. are clinically well, 7 per cent. are arrested and 23 per cent. are dead. Of the 17 partial collapse cases in this group, 6 per cent. are clinically well, none are arrested and 76 per cent. are dead. Of the 9 no-free-space cases, none are clinically well, none are arrested, and 97 per cent. are dead. Of the 30 cases in Clinical Group IV receiving pneumothorax treatment, 19 had demonstrable tuberculosis in the contralateral lung, and in 15 it was active. Progression took place in five cases but did not compel discontinuation of the pneumothorax.

In no class of cases is a satisfactory collapse so vital as in acute phthisis. A partial collapse is of much less value in this form than in any other. Caseation is considered by many a contraindication for pneumothorax, but according to our experience, it is not. However, in cases with progressive caseation and no tendency to softening, and with grave toxemia and in bad general condition, a pneumothorax is of doubtful value. Nevertheless, artificial pneumothorax is of great value in acute forms of phthisis, providing a satisfactory collapse can be established.

**CLINICAL GROUP V.**—This group comprised 30 cases of bilateral exudative, productive tuberculosis with demonstrable cavities in both lungs. All were far advanced cases (Stage III). Of the 30 cases in this group, 7 had a satisfactory

collapse and 3 (or 42 per cent.) are clinically well, none are arrested and 4 (or 57 per cent.) are dead. Of the 12 partial collapse cases 1 (or 8 per cent.) is clinically well, 2 (or 16 per cent.) are arrested, and 7 (or 58 per cent.) are dead. Of the 11 no-free-space cases, none are clinically well, 2 are arrested (18 per cent.), and 7 are dead (63 per cent.).

Bilateral cavernous tuberculosis has always been considered a contraindication for artificial pneumothorax. However, we withheld pneumothorax treatment until activity in the contralateral lung had largely subsided, leaving mostly a stationary cavity, and then the collapse was very gradually brought about, in many instances consisting of only a thin layer of gas between the lung and chest wall. Meanwhile, the opposite lung was carefully observed. All cases were selected with great care and most painstakingly observed. Clinical recovery by the usual sanatorium methods in this class of cases is quite uncommon. Consequently, to have restored a large proportion of these cases to health is certainly worth the effort and patience they require. Unfortunately, adhesions will prevent a satisfactory collapse in most cases of this type.

#### SUMMARY.

1. The most favorable results from pneumothorax treatment were achieved in the chronic fibrocaseous types of tuberculosis without demonstrable excavation, when adhesions did not prevent a satisfactory collapse, and with essential freedom from disease in the noncollapsed lung.

2. In the progressive fibrocaseous cavernous types, with lesions more destructive in character and more widespread, the end-results are correspondingly less satisfactory.

3. In actively advancing, caseous pneumonic and caseous bronchopneumonic types, in spite of statements to the contrary, one sees splendid results, providing a satisfactory collapse can be established and there are no contraindications. But in no class of cases is a satisfactory collapse so vital.

4. In bilateral fibrocaseous cavernous cases, providing the disease on the non-collapsed side is quiescent or at least not actively progressive, one often sees good results following collapse on the more diseased side, also providing a satisfactory collapse is obtained.

5. In desolate bilateral cases, according to our present views, a pneumothorax is justified as a palliative measure in only a few selected cases. The benefits are slight and never lasting, but it does often give relief from troublesome cough and hemoptysis.

6. In unilateral cavity cases, the sooner a pneumothorax is established, the better; not only is danger of intestinal infection diminished, but the possibility of bronchogenic extension on the same side and to the other side is lessened.

7. While it is desirable to have the disease confined to the one side, the presence of even active disease in the contralateral lung does not contraindicate pneumothorax treatment, provided it is not too extensive or of an acute infiltrating or rapidly advancing character.

Progression of disease more frequently took place in partial-collapse cases (9 per cent.) than in the satisfactory-collapse cases (4 per cent.). Improvement

in the contralateral lung is often coincident with and dependent upon improvement of the collapsed lung. Therefore, with disease on the opposite side, the odds are in favor of the patient that the disease will not progress, and especially if the collapse is satisfactory; and even in partial-collapse cases the odds are still in favor of the patient that the lesion will not progress.

The most serious type of contralateral lung disease is the fibrocaceous cavernous lesion. Disseminated bronchogenic caseous extensions in the contralateral lung are serious and, while less often provoked to progression than a fibrocaceous lesion, they are far more fatal.

Deep peribronchial and quiescent fibrocaceous lesions in the contralateral lung are relatively benign if a satisfactory collapse is established on the more diseased side.

8. Tuberculous laryngitis usually improves with improvement of the lung process and is not a contraindication *per se*.

9. Tuberculous enteritis, if interfering with the patient's nutrition and not responsive to treatment, is probably a contraindication for pneumothorax.

10. The "gas embolism-pleural shock" symptom complex occurred 19 times in over 20,000 inflations or attempted inflations, and in two cases was fatal.

11. Tuberculous empyema occurred in 12 per cent. of 480 collapsed cases, but it was not a serious complication unless open drainage procedures were established.

12. Serous exudates were demonstrable in practically every case at some time during the course of pneumothorax treatment, but as long as it remained serous it was never a serious complication.

13. Pleurisy with effusion on the noncollapsed side occurred seven times.

14. Progression of disease in the noncollapsed lung took place in 34 cases.

15. Adhesions are almost invariably present in cases demanding a pneumothorax and constitute the greatest obstacle to establishing a satisfactory collapse.

16. The results of treatment in the satisfactory-collapse cases and no-free-space cases indicate the justification of utilizing pneumothorax treatment earlier in the course of tuberculosis than has been generally customary. We feel that it is often a mistake to delay pneumothorax treatment and subject a patient to prolonged trial of sanatorium treatment.

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Minute and judicious consideration assures us of the importance of establishing the type of pneumothorax which, within four to six months, will give the diseased lung enough functional rest, collapse or compression to restore it to such state where it will no longer be a source of positive sputum or tuberculo-toxemia



Fig 1—Band adhesion preventing closure of large cavity. Pneumothorax of six months' duration with serous exudate formation. Sputum 50 c.c. T. B. positive and twenty-four hour quantity unchanged. Metastatic extension in contralateral lung. Consultation case—pneumolysis advised—other consultant advised continuation of pneumothorax.

The value of a satisfactory pneumothorax in cases where adhesions did not prevent the closure of cavities or adequate rest of the lung as compared with an unsatisfactory one in which adhesions did retard the mechanical and physiological benefits of a therapeutic pneumothorax is shown in Table 1. We do not sanction the too customary practice of continuing a useless pneumothorax over

lengthened periods, thereby denying the patient advantages of other operative procedures. In cases presenting adhesions, the method of attempting to obtain a satisfactory pneumothorax by means of stretching the adhesions by gradually increasing the intrathoracic pressure, is not only unsuccessful to a conspicuous degree, but accompanied with extreme danger. Frequently the adhesion is torn;

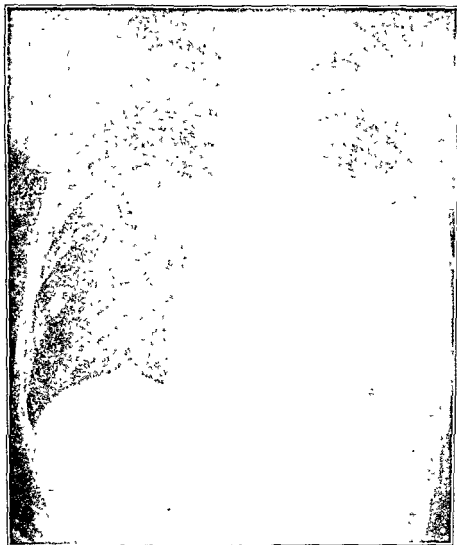


Fig 2.—Same case as fig 1. Four months later, after continuation of useless pneumothorax. Three weeks before exitus. Exudate purulent previous two months.

and because neither the position of the tear nor its extent are under control of the operator, any laceration may injure blood-vessels, the disastrous consequence being a hemorrhage. There is also the risk of its extending into the lung or prolongations of cavities extending into the adhesion, thus releasing infection, terminating in spontaneous pneumothorax and empyema. Our experience shows that spontaneous pneumothorax was 4 per cent. more common in pneumothorax cases presenting adhesions where high intrapleural pressures were necessary to

secure a good lung collapse, than in cases wherein adhesions were present, but did not prevent a satisfactory collapse of the lung and increased intrapleural pressure was needless.

Since opening of the pleural cavity for the purpose of cutting adhesions is not borne well by tuberculous patients, the procedure is not warranted by the



Fig. 3.—Caseouspneumonic tuberculosis with large cavity. Metastatic extension to contralateral lung. Afternoon temperature 102° F. Sputum 30 c.c. T.B. ++

results. If severing of adhesions by surgical methods comes into question, the closed method of intrapleural pneumolysis is undeniably far superior.

In selecting the closed method of approach, we have for consideration the closed intrapleural pneumolysis proposed by Jacobaeus<sup>1</sup> in 1913, utilizing the galvanocautery for cutting purposes; or, instead of the galvanocautery, the electrosurgical method,<sup>2</sup> utilizing a high frequency current, may be used according to the author's technic, which will be described later.

**Indications for Operation.**—The mere presence of adhesions *per se* is no indication for operation, for adhesions exist almost invariably in cases requiring pneumothorax treatment. In a great number of cases they do not conflict with a satisfactory collapse of the lung, and recourse to positive intrapleural pressures for the purpose of stretching them is unnecessary (Figs 3, 4 and 5).

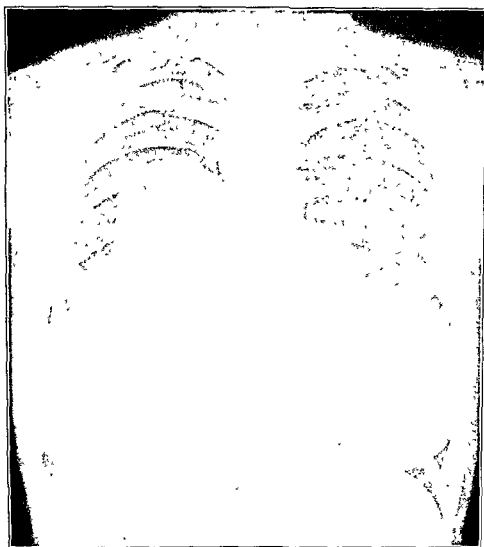


Fig. 4.—Same case as Fig. 3. One month later. Temperature normal Sputum 15 c.c. T.B. ++.

The first necessity is that the case be one in which, after a justifiable length of time (four to six months) it can be demonstrated that adhesions are preventing a satisfactory collapse of the lung and recovery is regarded doubtful with a continuation of the deficient pneumothorax. There should also be well-grounded conviction that the patient will recover, provided a satisfactory collapse of the lung is established. To epitomize, any extensive disease in the contralateral lung or in the intestines would, in all likelihood, prevent the patient's

recovery, even if a satisfactory pneumothorax were instituted; for this reason, it is essential that no serious complications exist.

The second requirement is that the pneumothorax cavity must be of sufficient size to facilitate manipulation of the instruments.

Additional indications for operation are, first, the adhesions preventing a satisfactory lung collapse must be of a reasonably suitable type for operation;

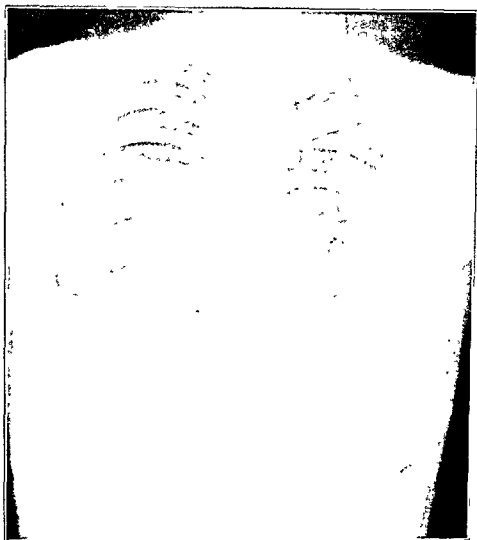


Fig. 5—Same case as Fig. 4. One year later, no cough or expectoration. Sputum T.B. negative for six months. Two years later patient married and is now clinically well.

second, satisfactory pneumothorax, in spite of adhesions of the above type, where high intrapleural pressure is necessary to maintain the collapse or compression with potential danger of lung rupture, or where the intrathoracic pressure is causing uncomfortable symptoms such as phrenic dyspepsia, from downward pressure on the stomach or liver; or coughing paroxysms, or pain from traction upon adhesions, circulatory disturbances because of altered position of the heart,

or traction of pleuropericardial adhesions, or because of pressure upon, or traction, or torsion of large blood-vessels, or marked mediastinal hernia. In some cases where adhesions are hindering the closure of cavities, and increased intrapleural pressures are resorted to, mediastinal bulging occurs, occasionally attaining considerable magnitude (Figs 6, 7, 8). Increased pressures, instead of producing better cavity collapse, cause only increase in the mediastinal hernia. Still

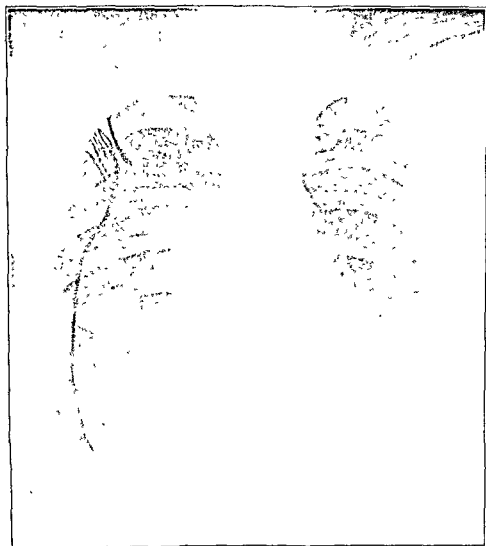


Fig. 6—Large band adhesion (retouched) preventing closure of cavity. Note downward displacement of the diaphragm

another indication for operation is a pneumothorax which has been satisfactory, but in which cords or bands of adhesions have become organized and are contracting, prompting early expansion of the collapsed lung (Figs. 9, 10, 11), in cases in which the pneumothorax has not been maintained long enough, or where recurrence of symptoms, such as increased sputum or reappearance of tubercle bacilli in the sputum, or hemoptysis has taken place.

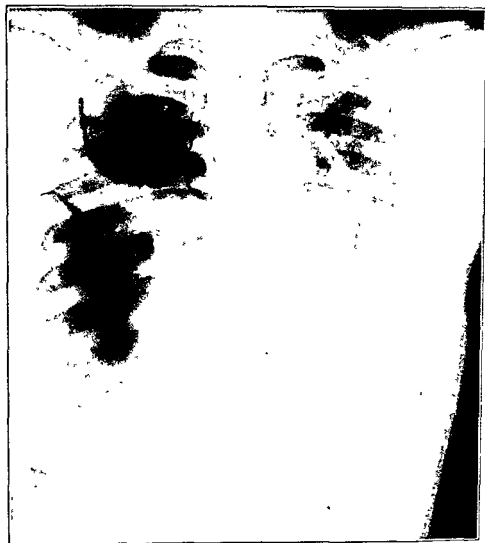


Fig. 7.—Same case as Fig. 6. Cavity closed. Note displacement of trachea, mediastinum and diaphragm.



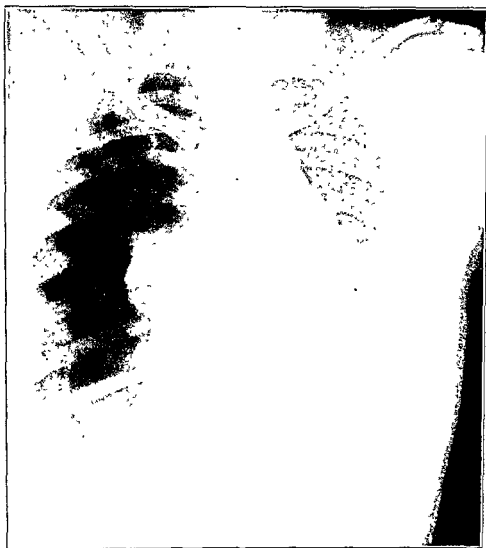


Fig. 8.—Same case as Fig. 7 Twenty-four hours after the offending adhesion was severed. Note the large lung stump.

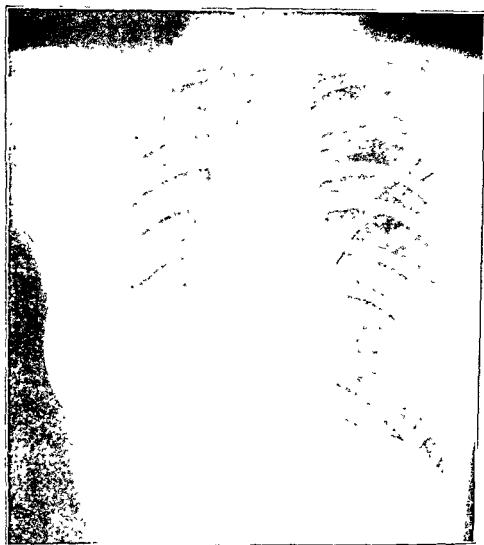


Fig 9—A satisfactory pneumothorax in spite of a band adhesion (retouched). Sputum negative.

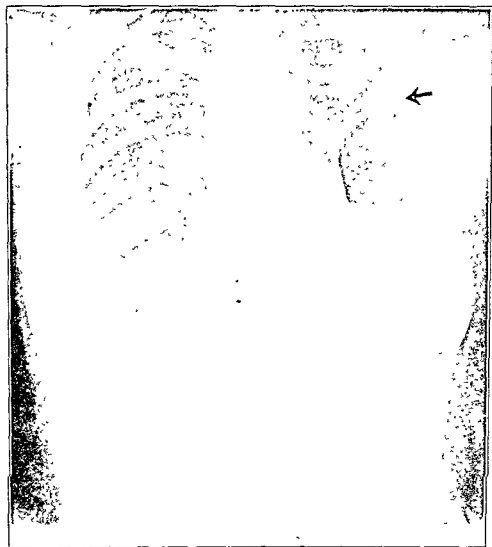


Fig. 10—Same case as Fig. 9. Nine months later—acute pleuritis with exudate. Adhesion contracting—lung re-expanding. One month later sputum became positive.

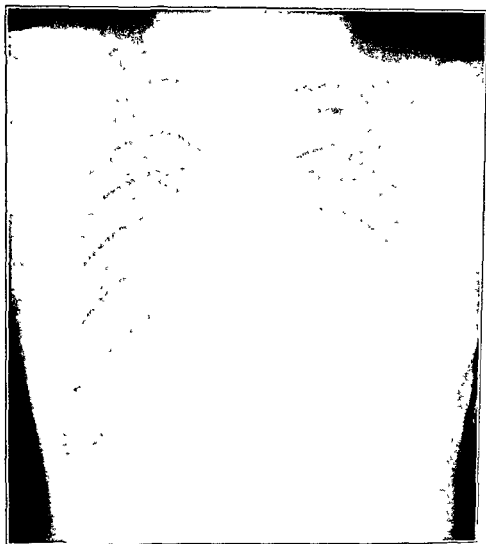


Fig 11—Same as Fig. 10 Twenty-two months after the band adhesion had been severed. Effusion treated by aspiration. Pneumothorax re-established. Sputum negative six weeks after operation.

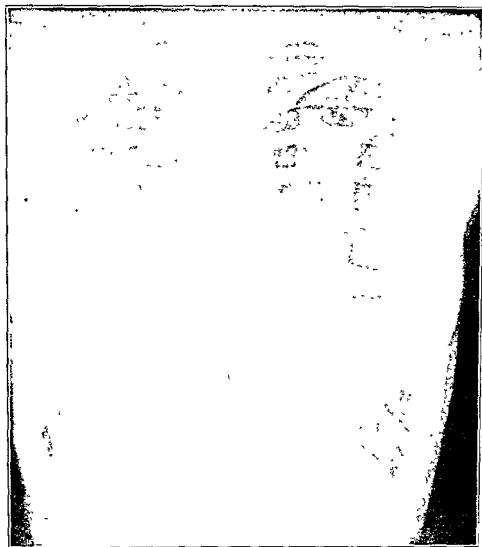


Fig. 12—Bilateral pneumothorax. Case referred for operation. Sputum 10 c.c. T.B. positive. Band adhesion preventing satisfactory collapse of the left lung.

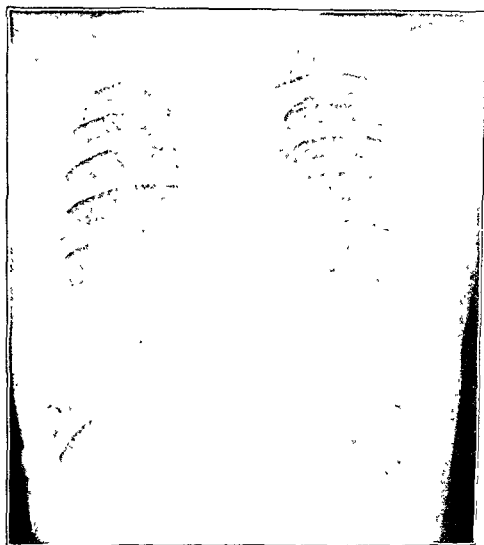


Fig. 13—Same case as Fig 12. Three days after severing band adhesion. One week later the patient had neither cough nor expectoration. Patient now ambulant with bilateral pneumothorax. Sputum negative two years.

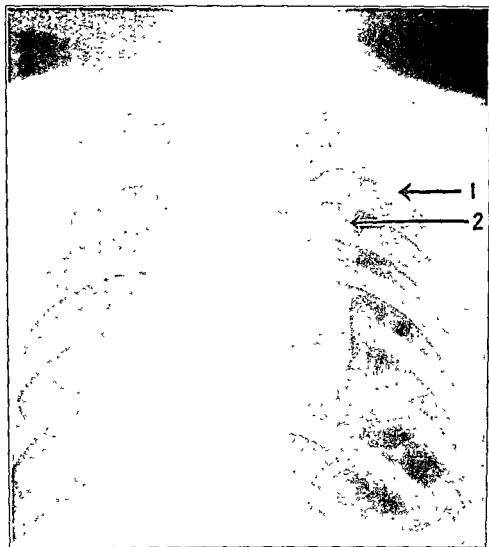


Fig. 14—Case referred for operation. Supposedly a band adhesion (1) prevented closure of a large cavity (2). Thoracoscopic examination revealed (1) to be the floor of a second large cavity

**Contraindications.**—Tuberculous disease in the contralateral lung is no contraindication *per se* for the cutting or cauterization of adhesions that prevent satisfactory collapse of a lung. Even a pneumothorax on the contralateral side is no contraindication, provided there are indications for bilateral pneumothorax (Figs. 12 and 13). Obviously, the contraindications otherwise are the same as



Fig. 15—Case referred for operation. (1) was thought to be an adhesion preventing a satisfactory collapse of the lung. Note the small pneumothorax with exudate.

those which apply for establishing a pneumothorax. The presence of benign exudate is no contraindication, as will be noted later. Severing adhesions should not be done during an acute formation of exudate. Acute pyothorax contraindicates operation, but chronic afebrile pyothorax is not a contraindication *per se*. Should there be an excessive amount of purulent exudate, the adhesion will have so dense a sheathing of purulent debris that the operator will be encumbered with the impediment of ascertaining the nature of tissue to be cut.



**Selection of Cases.**—The selection of cases for operation should be made only after a careful study of, preferably, stereoscopic roentgen films taken before the pneumothorax therapy is begun and during its entire course. Stereoscopic-film study is incumbent before operation, so that one may be perfectly familiar with the position of cavities in the collapsed lung and their likely correlation to



Fig. 16—Same case as Fig. 15. After aspiration of fluid and injection of skiagenol. Film made with the patient in a horizontal dorsal position. Thoracoscopic examination also revealed small pneumothorax with large uncollapsed cavity.

adhesions, as well as the location of adhesions and their attachments to the lung and chest wall.

A careful record of the influence of the pneumothorax on the twenty-four-hour quantity of sputum, as measured at weekly or monthly intervals, should be available. If the original film shows a superficial cavity, and serial films during the evolution of the pneumothorax divulge short adhesions holding the

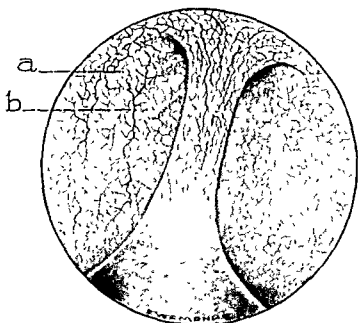


Plate I—Band adhesion attached to the chest wall near the subclavian artery and vein (a. Vein; b. Artery.) This type should be severed close to the chest wall attachment.

perfectly astonished at the number of adhesions found on thoracoscopic examination that were not shown on stereoscopic films at all. Therefore, it is well to remember that adhesions, evidently present but not visualized by the most careful roentgenological technic, are detected in nearly every instance at the time of operation.

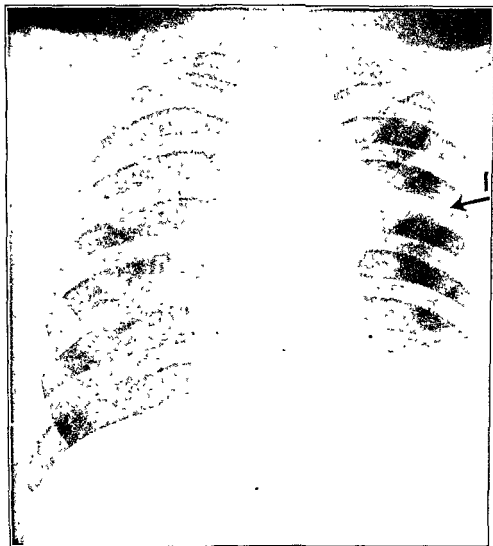


Fig 18.—Case referred for operation. Thoracoscopic examination revealed a thick fold adhesion (1) (which had been diagnosed a large band adhesion) extending across the costovertebral gutter to the lateral chest wall—it was inoperable.

Frequently, too, adhesions not shown on roentgen films are technical factors preventing collapse of the lung; my reference is to string adhesions of a consistency as tenacious as strings on a fiddle (and scarcely any larger), extending from the partially collapsed lung to the chest wall, and sometimes giving a tented contour to the lung incompletely collapsed. We encountered in one case, in which

there was suspected only a small band, numerous slender strings of the type alluded to above, and until severance, there was no lung collapse (Fig. 17).

An adhesion having all semblances of a band on stereoscopic films often proves to be a thick-edged fold adhesion (Fig. 18). In deciding upon the feasibility of operation and the degree of success, the most trustworthy method is certainly by thoracoscopic examination of the pneumothorax cavity. There should be no hesitancy in its utilization in any questionable case, since the procedure is in no way harmful.

### SURGICAL ANATOMY.

An accurate insight of the detailed and precise anatomy of the pleural cavity is absolutely indispensable to the thoracoscopist. But it is a prodigal anticipation to reckon upon seeing all the structures pictured in anatomical drawings, for many of these are not exposed until the pleura has been removed. The presence of the lung too (although it is partially collapsed, as in a pneumothorax), prevents such visualization; also, with prolonged pneumothorax treatment, or in some cases even after pneumothorax treatment of short duration, if a pleuritis occurs, the pleura becomes thick, and being no longer transparent, discrimination of vital structures frequently cannot be effected. In cases where the pleura is covered with fibrin, or a caseous pleuritis has become established, it is difficult to orientate oneself because rib, intercostal muscles, adhesions and lung parenchyma all appear to be of the same gross pathology.

The initial view, after having introduced the thoracoscope, will, of course, depend upon the completeness of the lung collapse. When the thoracoscope has been introduced with the lens up, in a recent pneumothorax with unthickened pleura, the first view is of the intercostal muscles and yellowish-white ribs: these necessitate no more than a cursory recountal, as they can be easily differentiated from other tissues. Rotating the thoracoscope so as to bring the lens downward, the lung is seen—its lobular markings are too evident to be erroneously interpreted. The borders of the lobes of the lung and the interlobular fissures are fully exposed to view, unless the lobes are adherent because of a previous interlobar pleuritis. Two distinct movements of the collapsed lung will be perceptible—one due to respiration, the other to cardiac systole and diastole. Considering that transmission of cardiac motion to adhesions occurs very often, the subsultory oscillation must not be construed as pulsation of blood-vessels within the adhesions. Sometimes adhesions will be present in the interlobar fissures, extending between the partially separated lobes of the lung; these should not be cut, as they are of no technical importance. The entire pleural cavity may be completely inspected by a simple rotation of the thoracoscope and altering its direction.

For the reason that the internal intercostal muscles are absent, and the endothoracic fascia gradually fades out of sight in the costovertebral gutter, the intercostal veins are quite conspicuous in this region and can be readily pursued for some distance in the intercostal space until they are lost in the rib sulcus. On the left side, the hemiazygos and accessory hemiazygos veins are promptly identified, as are also the internal mammary veins anteriorly. Unless one is an

experienced thoracoscopist, the artery is a bit awkward to identify because of the pronounced similitude of arteries to adjacent tissue. The sympathetic trunk and thoracic duct are seldom seen on either side; and the aortic arch (on the left side) is but rarely visible, as the lung in most cases obstructs the view and prevents visualization of the thoracic aorta. On the right side, the superior vena cava—also the right, and very frequently the left innominate vein, may be seen joining the superior vena cava. The ascending aorta was seen once in our series. The

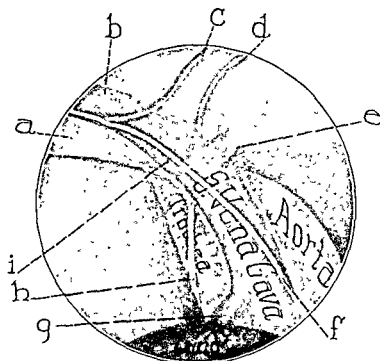


Fig. 19.—Thoracoscopic view of the right upper mediastinum and part of the pleural cupola.

- |                             |                          |
|-----------------------------|--------------------------|
| a. Subclavian artery.       | e. Left innominate vein. |
| b. Subclavian vein.         | f. Phrenic nerve.        |
| c. Internal mammary artery. | g. Hemiazygos vein.      |
| d. Internal mammary vein.   | h. Vagus nerve.          |
| i. Right innominate vein.   |                          |

Drawing made from actual case. (This is the only case in the author's series in which all of these structures have been visualized.)

vagus nerve is seldom seen on either side, but the phrenic nerve is easily recognized (Fig. 19). The trachea and esophagus may be noted on the right side. The azygos vein is seldom visible because of the lung.

A comprehensive knowledge of the pleural cupola cannot be stressed too forcibly because adhesions requiring cutting are frequently attached to this locality. The most noticeable and impressive structure in the cupola (Fig. 19) is a bluish ridge anteriorly: the subclavian vein. Pursuing it medially, the innominate vein is seen, and, on the right side, one marks its fusion with the superior vena cava. The subclavian artery, owing to its paleness, is not as plainly

discernible as the vein, but will be recognized as a throbbing ridge passing from the medial aspects of the cupola across the anterior part and eventually vanishing above the first rib. Branches of the brachial plexus are distinguishable in the cupola, and the costocervical artery can frequently be traced from the subclavian artery to the neck of the first rib.

On the left side, where the pulsating left ventricle shows distinctly through the pericardium (if it is not thickened), the heart is very self-evident. On the right side, the undulating movement of the right auricle is indubitable, but because of the lung, the hilus is seldom well seen. The diaphragm appears as

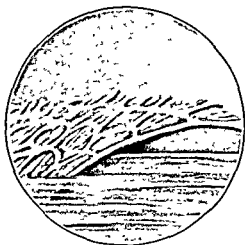


Fig. 20.—Thoracoscopic view of an arachnoid adhesion in the costovertebral gutter, partly submerged in exudate.

a reddish dome with a central grayish area—the central tendon. In an old pneumothorax, or recent one where a chronic pleuritis has existed, the pleura is often so much thickened that it is impossible to identify the ribs and intercostal muscles or any of the important vascular structures.

### PLEURITIC ADHESIONS.

Before describing the operative technic, a brief description of adhesions commonly met with at operation will be given. This classification is based upon extensive clinicopathological studies, the details of which will be described below. Other types of adhesions are found which are not included in these groups, but the classification will serve as one of great import to the beginner in avoiding accidents. While in some cases one type alone is perceived, one meets, in others, with a combination of many of those about to be described:

(A) **Arachnoid Adhesions** (Fig. 20).—This type is the result of a very recent linear pleuritis with profuse fibrin production. When very fresh, they separate readily without cutting, but after becoming older, they form into con-

nective tissue. These never contain lung tissue and are not of technical importance.

(B) **String Adhesions** (Fig. 21).—String adhesions are derived from small, circumscribed areas of recent pleuritis. While essentially round, they are occasionally flat and as a rule have only a slight increase in diameter at the

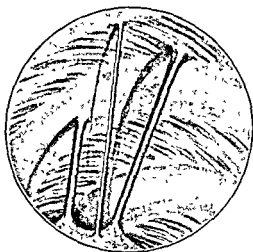


Fig. 21.—Thoracoscopic view of thin string adhesions extending between the lung and chest wall.

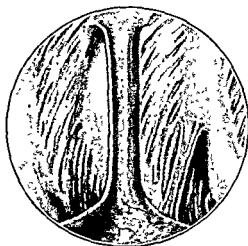


Fig. 22.—Thoracoscopic view of a round type of cord adhesion, and to its left a flat type of cord adhesion.

chest wall and lung attachments. They vary in size up to 5 mm. in diameter and may be many centimeters long. Some are frail, rupturing readily as the lung separates from the chest wall, while others are elastic and stretch easily. Still others are slightly vascular, and after a few months become quite compact and firm. They are of little clinical importance except when very numerous and fibrous (Fig. 17).



Fig. 23.—Short cord adhesion (1) in pleural cupola preventing closure of a large cavity (2). Note the mediastinal displacement (3).

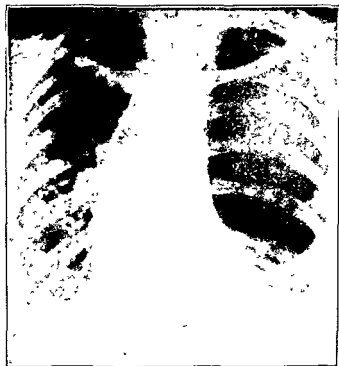


Fig. 24.—Same case as Fig. 23. Forty-eight hours after operation.



(C) **Cord Adhesions** (Fig. 22).—These adhesions have the same origin as the former group and have the same characteristics, except that they are larger, and while essentially round, at times show some ridging. The thoracic wall and lung attachments are often slightly broadened, especially when short, and might then be mistaken for spool or capstan adhesions.

Cord adhesions, unlike the string type, are of technical importance. Unless short and attached close to large blood-vessels, they are, however, seldom highly

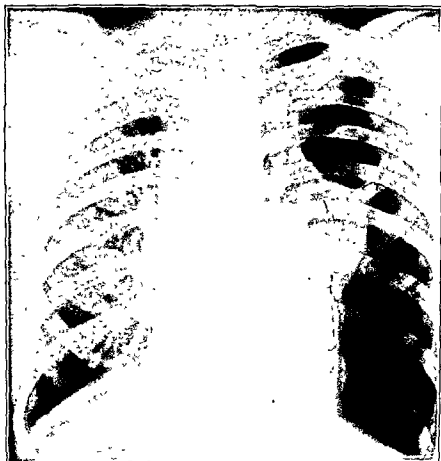


Fig. 26.—Pneumothorax of eight months duration. Sputum constantly positive and the twenty-four hour quantity uninfluenced. Band adhesion preventing closure of cavity.

vascular. Through critical observation, the author has found that a satisfactory collapse of the lung is prevented by even one cord adhesion, especially if its pulmonary attachment is over an uncollapsed cavity (Figs. 23 and 24).

(D) **Band Adhesions** (Fig. 25).—Band adhesions more often take their origin from an interlobar pleuritis, and if short, have a covering of pleura. They vary in thickness from a few millimeters to a centimeter or more, and their width may be from 1 to 10 cm. or more, and length from 1 to 10 cm. or more. At times they contain blood channels of marked significance, especially midst dense strands of fibrous tissue in old adhesions. They consist mostly of connective

tissue, and, except when short (a few centimeters), lung tissue is rarely embodied in them. Band adhesions are of great technical importance. Aside from bleeding, severance is not associated with danger. They must be severed close to the chest wall (Figs. 26, 27).

(E) **Fan-shaped Adhesions** (Fig. 28).—This form arises from an old pleuritis, very often the result of conglomerate tubercles extending to the pleura.



Fig 27.—Same case as Fig 26 Ten days after operation. Closure of the cavity took place at once. A positive sputum was never obtained until one and a half years later, when the opposite lung became active.

Small blood-vessels are often contained in the free edge. The transition between lung tissue and adhesion is clearly defined. This flabelliform type seldom contains lung tissue, and they should always be severed near the lung attachment rather than at the chest wall. Cutting is not associated with danger, and a good therapeutic result follows.

(F) **Funnel or Cone-shaped Adhesions** (Fig. 29).—This form differs markedly from the fan-shaped type in that it has a broad, round, visceral end with a slight, usually round, thoracic attachment. Adhesions of this type result from old, circumscribed areas of pleuritis, causing intimate attachment between

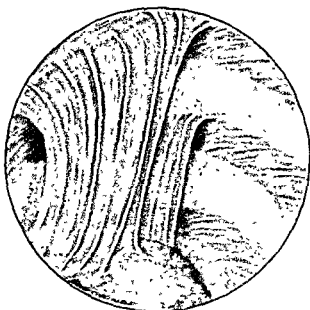


Plate II—Complex type of band adhesion in a recent pneumothorax. It is not highly vascular and should be severed near its chest wall attachment.

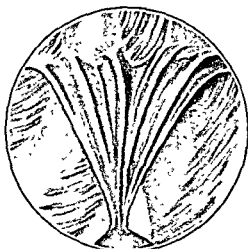


Fig. 28—Thoracoscopic view of a fan adhesion extending between the lung and chest wall

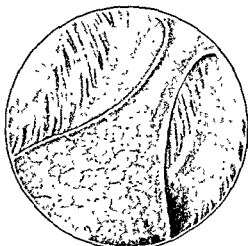


Fig. 29.—Thoracoscopic view of a funnel or cone adhesion containing the prolongation of a cavity

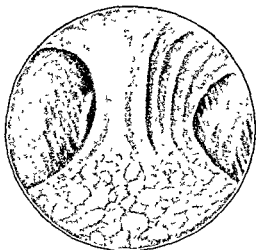


Fig. 30—Spool adhesion in pneumothorax of a four months' duration. The chest-wall attachment is highly vascular. The lung attachment contains prolongations of lung tissue. It was severed close to the chest wall without hemorrhage



Fig. 31.—Case referred for operation. Spool adhesion (1) preventing closure of cavity (2). Pneumothorax with exudate one year. Two weeks previously an attempt had been made elsewhere to sever the adhesion, but it was considered inoperable.

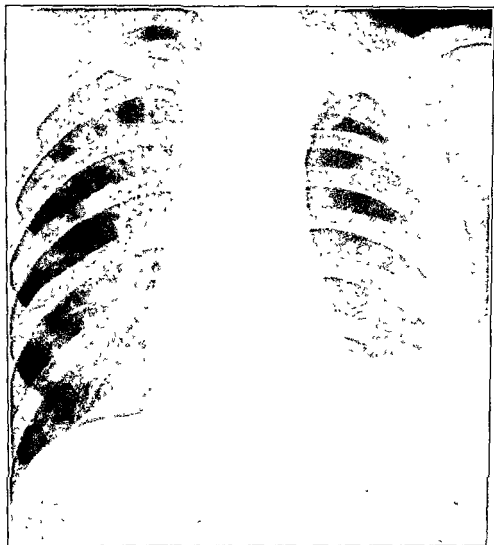


Fig. 32.—Same case as Fig 31. One month after operation cavity closed—lung satisfactorily collapsed—exudate formation not aggravated—contralateral lung not aggravated

the visceral and parietal pleura. They usually occur over superficial cavities, in which case the cavity is often projected into the base of the adhesion. Following prolonged pneumothorax treatment, the pleura becomes thick and the conformation of the adhesions cannot be presaged—it is imperative to bear in mind, then, that this shape always contains lung tissue and often the prolongation of a cavity. Cutting an adhesion of this form, unless around the chest wall attachment, is dangerous. If successfully operated upon, splendid therapeutic results are obtained.

(G) **Spool or Capstan Adhesions** (Fig. 30).—These adhesions are composed of lung parenchyma pulled out in a *funnel* shape and compressed into a *spool* shape, and also contain connective tissue. They result from old, circum-

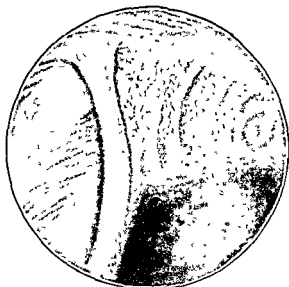


Fig. 33.—Curtain adhesion in the costovertebral gutter.

scribed areas of exudative pleuritis with obliteration of the pleural space. When older, they may contain blood channels of considerable size. Sometimes prolongations of cavities are present and lung tissue is always found in the pulmonary attachment.

By the change of color, lung tissue can be traced up to (and sometimes beyond) the narrowest point of the adhesion. Although these are less dangerous to cut than the funnel-shaped type, the operator often has the same dangers to contend with. They should be cut as near the chest wall as possible and not at the narrowest point (Figs. 31 and 32).

(H) **Fold and Curtain Adhesions** (Fig. 33).—This form commonly arises from an interlobar pleuritis extending to the parietal pleura and becoming fixed. Following pneumothorax treatment, the lung may be compressed into a thin curtain. These adhesions are most generally distributed in the costovertebral gutter (Figs. 34 and 35), at the site of the interlobar fissures and often shown only on lateral films, but also are seen at the apex. They frequently appear as a



Fig. 34.—Large uncollapsed cavity in a pneumothorax of over one year's duration. Note large mediastinal hernia (*x x x*). No adhesions were seen on anteroposterior films.





Fig 35—Same case as Fig 34 Right anterolateral film showing fold adhesion in costovertebral gutter. Thoracoscopic examination revealed them inoperable.

band on stereoscopic films and give the impression of being easily cut. In a recent pneumothorax, lung tissue may be visible; when old, the adhesion becomes pale and dense, with an absence of lung markings.

Technically, these adhesions are very important and ordinarily responsible for many pneumothorax failures. From a surgical standpoint, they are mostly nonoperable. When thick, they should not be cut; when thin, they may be cut near the thoracic wall with extreme caution.

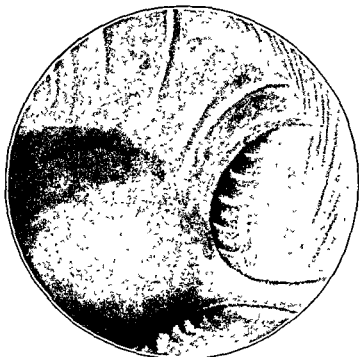


Fig. 36.—Thoracoscopic view of a diffuse adhesion containing lung tissue up to the chest wall. To the right is a large cord adhesion.

(1) **Diffuse Adhesions** (Fig. 36).—These adhesions arise from a more generalized pleuritis. The lung is closely adherent to the chest wall to which, in places, vestiges of lung tissue may be traced. In other localities they may be comprised largely of connective tissue, presenting numerous ridges and depressions. Extensions in the form of thin partitions may radiate from the main body of the adhesion, diverging to every point. Technically, they are responsible for more failures in pneumothorax than any other type of adhesion; surgically, their complete cutting should never be attempted.

#### PREOPERATIVE PREPARATION OF THE PATIENT.

The patient is prepared as for a major thoracic operation. If the pleural cavity contains a purulent exudate or oil of gomenol, it should be washed out with salt solution before the puncture. Exudate, if present, except in very small quantities, should be aspirated a few days before operation and a pneumothorax refill given at this time, if necessary, to furnish as large as possible a pneumo-

thorax in which to work. If a febrile reaction follows aspiration, the operation should be postponed until no reaction ensues.

Determination of the bleeding and coagulation time of the blood, as well as bloodgrouping, should be done. By instilling confidence in the painlessness of the procedure, the patient is psychically adjusted for operation. His coöperation

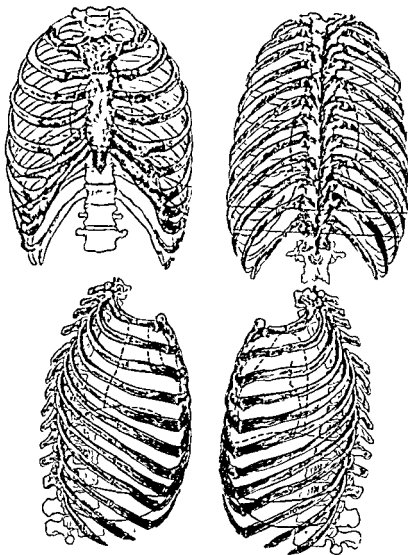


Fig 37.—Diagram of the thoracic cage utilized for charting character, position and number of adhesions, with relation to the collapsed lung and bony framework. Determined by stereoscopic film study for pre-operative guidance

to prevent moving and unnecessary coughing during operation is of extreme moment. Should the patient be anxious, a mild sedative may be given the night before operation to insure a good sleep, and sputum drainage must be carried out the morning before operation so as to prevent excessive coughing during and immediately after operation.

For preoperative medication, one may give morphine sulphate, Gr.  $\frac{1}{6}$  to  $\frac{1}{4}$ , with or without scopolamine, Gr.  $\frac{1}{200}$ . We have also resorted to sodium amytal, intravenous, in hypnotic doses in cases where extensive cutting was necessary.

A record of the stereoscopic film findings should be on hand. The author has found it very useful to sketch the position and direction of adhesions on a blank form of the thoracic cage (Fig. 37).

*Position of Patient on the Table (Fig. 38).*—This will depend upon the site of the adhesions.

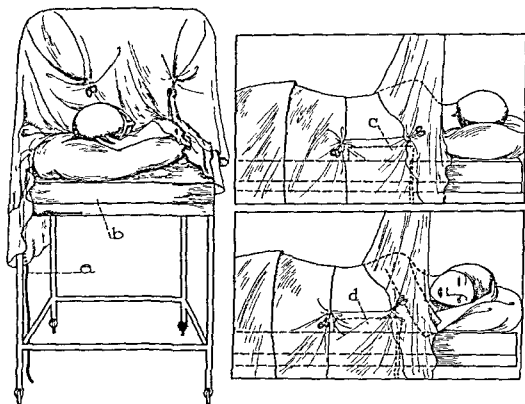


Fig. 38—Position on table of patient draped for operation.

a Cable connecting inactive electrode with high-frequency unit.

b. Cellular rubber pad.

c.-d. Anterior and posterior views of inactive electrode molded to the patient's side and secured by adhesive plaster.

### TECHNIC OF THORACOSCOPIC EXAMINATION.

The instruments required for thoracoscopy (Fig. 39) are a thoracoscope with a transformer to control its illumination, and a bakelite cannula with a trocar, by means of which the thoracoscope is introduced through the thoracic wall. After working with numerous thorascopes, both direct and indirect, as well as operating thorascopes, we believe the Unverricht thoracoscope is the best for general use. It is employed routinely by us, as it meets all the demands of a perfect instrument.

*The Author's Trocar and Cannulas for Introducing the Thoracoscope and Operating Electrodes.\**—The trocar is provided with an adjustable hollow handle, which renders the length of the trocar adjustable to the different lengths of cannulas. There are to be had three different lengths of cannulas, according to the thickness of the chest wall, as determined during the infiltration anesthesia. These cannulas are made of bakelite, which prevents short-

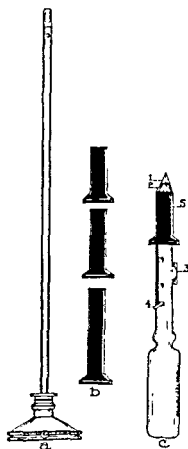


Fig. 39.

- a. Unverricht Thoracoscope.  
 b. Three lengths of bakelite cannulas.  
 c. Author's adjustable trocar (1) Solid short point. (2) Expanding flange holding bakelite cannula in position. (3) Lever controlling length of cannula. (4) Lever controlling flange (2). (5) Short bakelite cannula on trocar ready for use.

circuting of the high-frequency current to the chest wall. The lumen is of a size that permits entry of either the thoracoscope or operating instruments—an advantage noted later. They are nonflexible and should be sterilized in the formaldehyde chamber in the same manner as the optical instruments.

Adhesions, in the greater proportion of cases, will be found in the posterior upper quadrant of the pneumothorax cavity, and the point of entrance of

\*Manufactured by Carl M. McKissick, 71 East 6th St., Portland, Oregon.

the thoracoscope will be decided upon after assiduous study of the stereoscopic films. Because of the thickness of the muscles in the interscapular region and narrow intercostal spaces, it is best to refrain from utilizing this area. One seldom need go higher behind than the sixth or seventh intercostal space. If a higher approach is necessary for apical adhesions located anteriorly, the thoracoscope can be introduced anteriorly in the first or second intercostal space. In our series of cases, 90 per cent. of adhesions of technical importance have been above the fourth rib, in the posterior upper quadrant of the pneumothorax cavity.

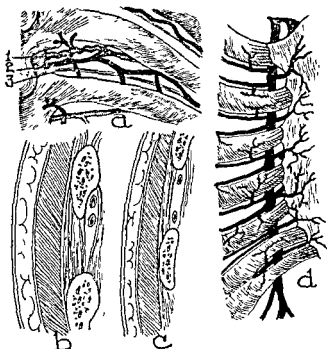


Fig. 40.

- a. Location of intercostal vein (1), artery (2) and nerve (3), in the costovertebral gutter, not protected by the rib.
  - b. Intercostal vessels posterior to axillary line, protected by the rib.
  - c. Intercostal vessels anterior to axillary line, not protected by the rib.
  - d. Internal mammary and intercostal artery anterior, not protected by the rib.
- (Modified from Sauerbruch and Gray.)

In 66 per cent. of our cases, the thoracoscope has been introduced posteriorly at the angle of the scapula; in 14 per cent. it was introduced anteriorly; in 20 per cent. it was introduced laterally. We prefer the posterior approach, for most adhesions can be examined more readily and extensively from this point, and because the intercostal vessels here lie in the rib sulcus, they are well protected from injury during introduction of the trocar and cannula for the thoracoscope (Fig. 40). The anterior approach for the thoracoscope is never used by the author, except in cases of apical adhesions anteriorly located.

The surgeon must satisfy himself beyond a doubt that the lung is not adherent to the chest wall, or that an adhesion not shown on the roentgen film is not attached at the point of entrance selected for the thoracoscope. Also, it is

of paramount importance to know whether the lung, if not adherent, is sufficiently far from the chest wall, or, if an adhesion should be present, that the intervening space will afford proper manipulation of the thoracoscope. In introducing the thoracoscope too close to an adhesion, there is no possibility allowed for examination of all its surfaces; needless to cite, such an occurrence at the outset of the operation is indeed most annoying.

These impediments are surmounted by a preliminary sounding of the pneumothorax cavity at the site selected for introduction of the thoracoscope (Fig. 41). A blunt Solomon pneumothorax needle and cannula are used for this purpose.

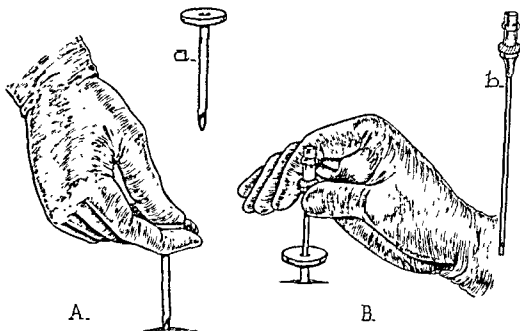


Fig. 41.—Method of sounding pneumothorax cavity to determine the distance of the lung from the chest wall and presence of nearby adhesions.

A. Introducing the cannula (a).

B. Sounding the pneumothorax cavity with blunt pneumothorax needle (b).

After introducing the cannula, the blunt needle is passed through it and the cannula withdrawn up the shaft of the needle. One then palpates carefully with the catheter in all directions for lung and adhesions, making exact citations of their distances. This procedure excludes resultant injury from thrusting the trocar for the thoracoscope into the lung or into adhesions at the location of the puncture.

Local anesthesia for the introduction of the thoracoscope is similar to that for a pneumothorax (a 1 per cent. novocaine suprarenin solution). The pleura must be approached with utmost consideration for the lung may be close to the chest wall and be inadvertently punctured. Careful infiltration of the endothoracic fascia is essential. To preclude disturbing and objectionable bleeding from a vascular pleura the use of suprarenin solution in the novocaine is a preëminent factor. The intercostal space being used must be injected with 10 to 20 c.c. of the

solution, but it is superfluous to anesthetize the intercostal spaces above and below the site of puncture. The incision through the skin should be about one centimeter long and made in the direction of the external intercostal fibers.

*Technic.*—If the site selected is found suitable for operation, the trocar and bakelite cannula for the thoracoscope are gently pushed through the chest wall in a horizontal direction (Fig. 42). The outer end is depressed and the tip of the instrument directed upward, thus avoiding the trickling of blood from the chest wall wound down the shaft of the cannula to the inner end which might later smear the lens. A thickened pleura, obviously, is characteristically unyielding—to avoid plunging the trocar through it, the most infinite care is essential, as the slightest default can be productive of great harm.

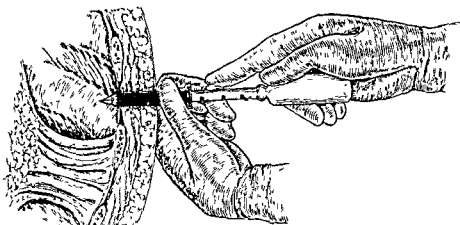


Fig. 42.—Introducing the author's trocar and bakelite cannula. The cannula is supported by the thumb and first finger to prevent its sudden plunge through the chest wall.

Having confirmed that the thoracoscope is in perfect order, the room is darkened and the trocar withdrawn; next, the thoracoscope is introduced in a horizontal direction, with lens up, so as not to foul it with an occasional drop of blood which may run down the cannula from the chest wall puncture and cling to the lower edge of its rim. After waiting a few seconds for water of condensation to disappear from the surface of the lens, a general survey of the pneumothorax cavity should be made, noting especially the vascularity of the pleura, and its thickness, the presence of fluid in the pleural cavity, fibrin deposits and tuberculous changes of the lung and parietal pleura, as well as the distribution of adhesions, their character and any changes in the pericardium. A well-devised estimate of the adhesions should purvey complete orientation regarding their position and direction with relation to the chest wall and collapsed lung—also their dimensions, configuration and distance from the lens and other anatomical structures. Adhesions will appear in their actual form and size as viewed through the thoracoscope when the instrument lens is parallel with the structure. It is particularly essential that the operator be familiar with the proximity of the point selected for cutting to large blood-vessels and important nerve trunks—such as the brachial plexus and the sympathetic trunk. After an exhaustive scrutiny has been carried out for contingent lung tissue, blood-vessels and tuberculous deposits



in the adhesion to be cut, the inner chest wall is studied and a suitable location decided upon for entrance of the electrode—one that will give a liberal perspective, and thereby admit placing the cutting instrument in the most advantageous position across all important adhesions at a right angle for the purpose of cutting. One must especially avoid introducing the electrode at a point where adhesions prevent its being seen, as, for instance, on the blind side of adhesions (Figs. 43 and 44) which have been selected for introducing the thoracoscope

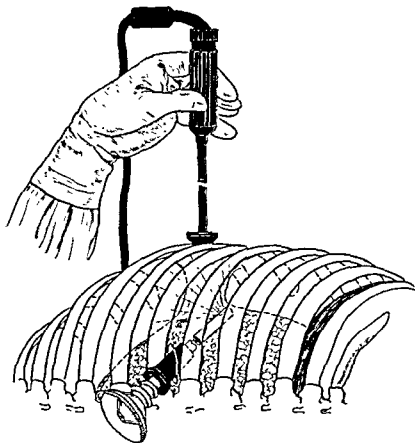


Fig. 43.—Incorrect position of operating electrode—the band adhesion prevents its visualization.

Usually, the pneumothorax side will be up, but it is not desirable to place a hard pillow beneath the patient for the purpose of widening the intercostal spaces, as the patient must be made as comfortable as possible, because the operation may last an hour or even longer and it is essential that the patient remain quiet. Consequently, we place a soft pad upon the operating table; beneath this is a two inch cellular rubber pad which adds to the patient's comfort and prevents grounding of the electrical current with the table. The patient's arms and legs, or any other portion of the body, should not be closer than one inch from the metal parts of the table. Before draping the patient, as shown in Fig. 38 *b, c*, an inactive electrode, consisting of a rectangular piece of diathermy metal, 10 inches  $\times$  12 inches, is fastened to the patient's chest with adhesive plaster.

This metal piece is connected with the unit by means of a cable. The operator should wear shoes with rubber soles or stand upon a dry wooden frame or rubber mat.

The point of entrance of the electrode will, of course, be dependent upon the thoracoscopic findings. In 70 per cent. of our cases, the electrode has been introduced between the anterior and midaxillary lines; in 25 per cent. it was introduced in the midclavicular line; in 5 per cent., the cutting instrument was introduced posteriorly. We find that because, in the majority of cases, the thoracoscope will be most advantageously introduced at the angle of the scapula, the anterior axillary line will naturally be a commodious site for introducing the electrode, as the intercostal spaces are now narrow and there is more freedom for

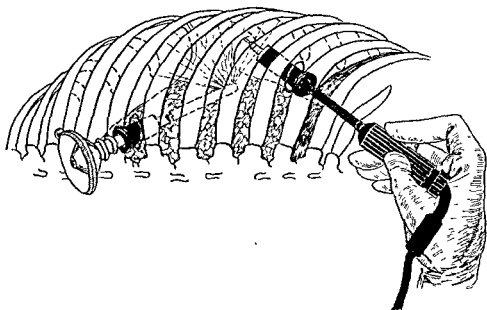


Fig. 44.—Correct position of operating electrode and thoracoscope.

guiding and regulating the instruments; their analogous position, too, is very good.

**Methods of Cutting Adhesions.**—Two are available—the *Jacobaeus method*, utilizing the galvanocautery, and the *author's method*, or *electrosurgical method*, utilizing a high-frequency current. There is a marked variation in these two methods, both in the form of instruments used for delivering the burning or cutting electrical current, and in the kind of electrical energy employed for burning and cutting. However, the operative technic for introducing the galvanocautery is the same as that followed when the author's electrode is used in the electrosurgical method.

The unpleasant features associated with cauterization of adhesions by the galvanocautery are the immoderate heat, smoke, pain and decided reaction after operation. The most prominent deficiency of this method is possibly the unfavorable nature of its cutting: destruction of tissue around the cautery frustrates any previous obliteration of blood-vessels—thus, they are severed, and excessive

bleeding may take place unless a dull red heat (dark room observation) is used. To augment the danger of hemorrhage, if an undue amount of heat is used, there is also the impending hazard of tissue necrosis occurring, which may well implicate the lung parenchyma, tuberculous cavities, or tuberculous foci, and in that way spontaneously discharge infection. Likewise, a secondary hemorrhage of a distressing character may be produced should the necrosis obtrude into blood-vessels. Another detrimental phase of the galvanocautery is the period of time required for the cautery to heat and cool; although this interval (as the current is thrown on and off) is very brief, sometimes the fraction of a moment's delay in rendering the cutting instrument active or inactive may result in alarming consequences. Aside from these defects, the cautery occasionally becomes very hot and may cause sloughing at the point where it passes through the thoracic wall. The hot shaft of the cautery may also injure the pericardium or lung tissue on which it may rest, unnoticed by the operator, who is concentrating his vigilance upon the tip of the cautery, burning an adhesion at a distant point. If one has to deal with a large adhesion, the heat of the cautery shaft, as well as the smoke engendered from burning often necessitates incessant pauses in the operation. This increases the duration of the procedure which at times becomes tiresome for both the patient and surgeon if much burning is required; furthermore, the pain from the heated cautery and reaction to operation, caused by the chemical changes which tissue proteins undergo at the site of cauterization, are a disagreeable element. These obstacles and dangers are every one momentous and have been stumbling-blocks thwarting a desirable outcome in numerous instances when the galvanocautery was employed for extensive operations.

Because of the obvious objections to the galvanocautery and the success of electrosurgery, especially in brain and cancer surgery, it seemed very probable that this method could be applied intrathoracically with excellent results. In 1927, I began studies of this method, which required the development of technic and instruments; these are now—after more than five years' application—sufficiently perfected and tested to offer as definitely superior to the galvanocautery method.

In adapting the electrosurgical method for closed intrapleural pneumolysis, disadvantages of the galvanocautery have been eliminated and certain specific advantages achieved by the use of this more modern and adaptable cutting medium.

**The Electrosurgical Method (Author's Method).**—In this method of cutting adhesions, a high-frequency current, which changes its direction of flow at the rate of upwards of a million times a second, is employed. Because of the rapid rate of alternation of current flow in this kind of current, there is no electro-chemical action and almost no neuro-muscular response. There is also an absence of electrical shocks, chemical action, and molecular changes, as well as the lethal effects associated with the ordinary steady or alternating commercial electrical current of much lower frequency.

The effects obtained by the high-frequency current used in electrosurgery differ markedly from the galvanocautery. In the latter type, the application of heat is made by a hot object and only superficial permeation achieved because

of carbonization of tissue, while the effect obtained by the electrosurgical method depends totally upon either the heat developed by the current in passing from the active electrode into the tissues, or upon the ohmic heat developed by the current in passing through the tissues (Bovie); the amount of heat is proportional to the square of the current density, and its depth of cell destruction is proportional to the strength and kind of current used. If the amperage is increased, more heat is developed and the effect carried much deeper, and heightened voltage offers added force with which to carry the amperage.

*The Current Density.*—A high current density is achieved by utilizing a small active or operating electrode, whereas, the inactive or indifferent electrode placed elsewhere on the patient's body is made large. The current, as a result

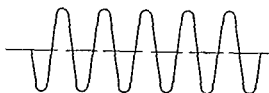


Fig. 45.—Undamped wave; will cut but has very little dehydration effect

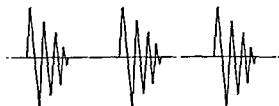


Fig. 46—Highly damped wave, will not cut but has excellent coagulation or desiccation qualities.

is concentrated in the immediate vicinity of the active electrode and rapidly decreases as the current passes from the active electrode through the patient's body to the inactive electrode.

Two distinct types of high-frequency current are employed in electrosurgery: one, an undamped current, or continuous wave current, which alternates in the direction of flow at a sustained, uniform rate and amplitude, and its delivery of energy is virtually uninterrupted; whereas, the other is a damped current which has intermittent deviations in rate and amplitude, and its energy occurs in recurrent discharges of considerable intensity—these existing, however, only transitorily—with inactive periods between the individual wave trains. Primarily dissimilar, these two types of high-frequency current manifest quite different effects in the tissue. The undamped current has cutting effects, but may also be used to heat the tissue, while the damped current is not capable of cutting, but desiccates or coagulates tissue (Figs. 45 and 46).

*High-frequency Apparatus.*—Numerous high-frequency machines are supplied today, including many portable "cutting machines," some operated on a spark-gap principle, others on the radio-tube principle. The construction of these is far from being the same, and currents produced by them are also of cor-

*responding varieties and qualities. Therefore, simply because the current delivered may be high-frequency, does not necessarily imply that it is applicable to electro-surgery, especially for cutting pleuritic adhesions: a pure, undamped current, although proficient for cutting, has very slight dehydration influence on severed tissue edges. This deficiency occasions bleeding very nearly the same as tissue severance with a scalpel, so it is palpable that a current of that type cannot meet*

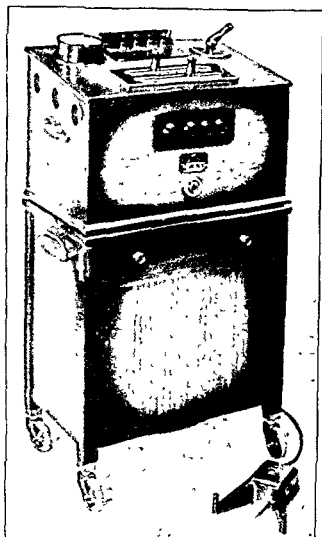


Fig 47—Universal Bovie electrosurgical and diathermy unit (latest model).

the rigorous exactions of intrathoracic surgery because of the incessant danger of bleeding and its incapability to cope with such a serious emergency. Due regard must be conceded to the fact that a hemorrhage intrathoracically cannot be controlled by procedures such as are utilized in open operations.

High-frequency units delivering pure cutting and pure coagulating currents are available, and though they are an advance over the galvanocautery, control of bleeding is very precarious. In the author's earlier experience with electro-

surgery, this type of unit was employed; it was disqualified because of its inability to cope with hemorrhage. During the course of operation, it was necessary to use the coagulating current first before the cutting current and repeatedly shift from one current to the other. This, of course, demanded annoying intermissions, and control of bleeding was most unsatisfactory.

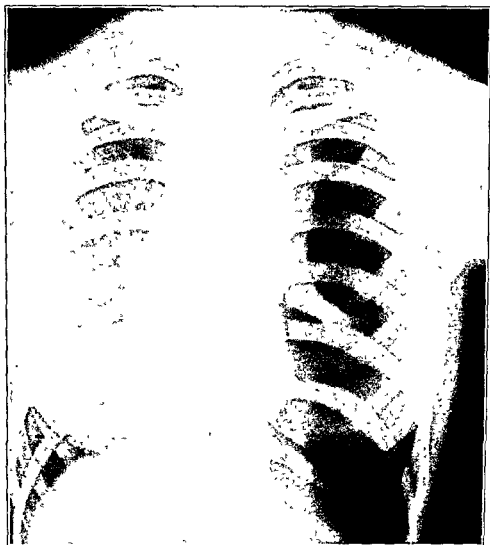


Fig. 48.—Pneumothorax of nine months' duration. Sputum constantly positive and unvarying in quantity for six months. Note mediastinal hernia and displacement of the diaphragm. Funnel adhesion is shown attached to the anterior end of the fourth rib—two band adhesions appear above the second rib.

After trying out several high-frequency machines popular in general surgery, we adopted the new Bovie electrosurgical unit\* (Fig. 47) in August, 1929, and find it meets all requirements. It offers the express advantage of three separate and distinct degrees of dehydration qualities while severing tissue, and is a com-

\*Manufactured by the Liebel-Flarsheim Co., 303 West Third St., Cincinnati, Ohio. (We have recently used the less expensive portable Bovie Unit and find it perfectly satisfactory.)

bination current which in wave form is somewhere between a pure undamped wave and the highly damped wave ordinarily supplied from a spark-gap machine. This unit supplies a new form of electrosurgical current, which has both cutting and coagulating properties. The employment of the Bovie unit has been conducive to much peace of mind because of insured hemostasis.

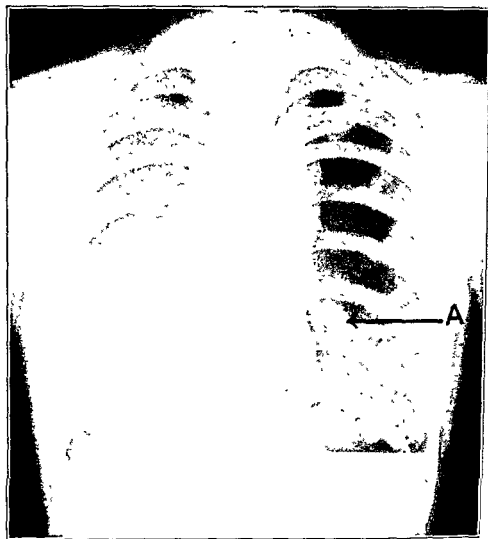


Fig. 49.—Same case as Fig. 48. Twenty-four hours after operation. The band adhesions above were severed. An attempt was made to sever the funnel adhesion (A) at the chest wall but severe bleeding occurred which was arrested by electrocoagulation. Note entire chest-wall attachment was thoroughly electrocoagulated.

High-frequency currents are employed for three separate purposes in the electrosurgical methods of cutting adhesions: first, superficial dehydration; second, coagulation; third, cutting.

*Superficial Dehydration.*—The type of high-frequency current least employed for severing adhesions is serviceable in some cases of band and fold or curtain

adhesions as a preliminary preparation to cutting, if the adhesions are very thin and vascular. To do this, either the cutting or coagulating electrode (depending upon the width of the desired path) is held a short distance from the tissues so that sparks are sprayed between the tissue and electrode; then the electrode is gradually moved in the line of the proposed cutting. A line of superficial

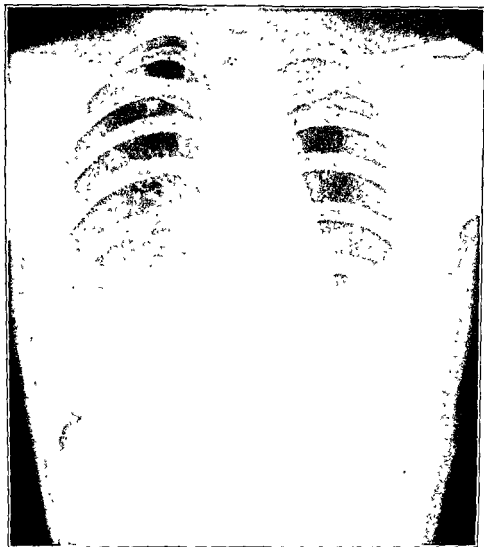


Fig 50.—Same case as Fig. 49. One month after operation. One week after operation the adhesion separated from the chest wall. The sputum became negative three months after operation.

dehydration of the tissue results from the high temperature of the sparks. Through the middle of the dehydrated zone, the cutting is now executed.

*Coagulation.*—This is widely employed as a preliminary preparation to the cutting of all adhesions having the appearance of vascularity or where vascularity is suspected though not visible—for instance, in the thick portion of band adhesions, fold or diffuse adhesions, or in the interior of cord, funnel and spool



adhesions attached close to large blood-vessels, especially if situated close to the internal mammary or subclavian vessels or in the costovertebral gutter. When many adhesions are present, and a number of operations are essential, or where adhesions are highly vascular, coagulation is recommended for the ones left for future operation. After a few days, a separation or stretching (Figs. 48, 49, 50) often begins, precluding the necessity of a second cutting operation.

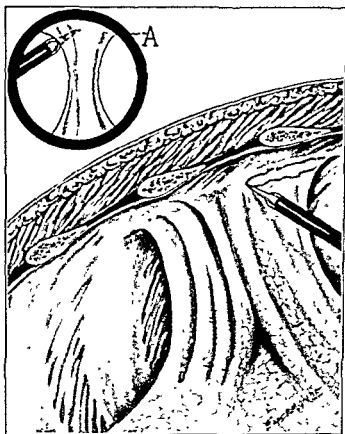


Fig 51.—Method of electrocoagulating chest-wall attachment of an adhesion containing lung tissue up to the chest wall, as well as the prolongation of a cavity. (Line of coagulation is shown)

*A. Insert showing position of pointed electrode at the chest wall.*

In dealing with funnel and spool adhesions which are thought to contain lung parenchyma or the prolongation of a cavity (and possibly blood channels), electrocoagulation surpasses every other method. Cutting the above types of adhesions close to the chest wall is assumed with timidity because of the danger of bleeding, and in cutting farther away from the chest wall, the possibility of cutting into a cavity or lung tissue is imminent too. It is often very difficult to come to a conclusion regarding the nature of the tissue to be cut in an old pneumothorax with thickened pleura; also efforts to effect a lung collapse with even high intrathoracic pressures are defeated by the thickened pleura. In this type of case, we find that a determination, first, of the thickness of the pleura is

essential—it can be done very simply with the needle of the infiltrating syringe; next, the chest wall base of the adhesion is circumscribed with a path of electrocoagulation of sufficient depth to penetrate the pleura only (Fig. 51). Carbon dioxide and air reinflations are then carefully begun as soon as the chest wall punctures are sealed (24 to 48 hours). After a few days the adhesion separates

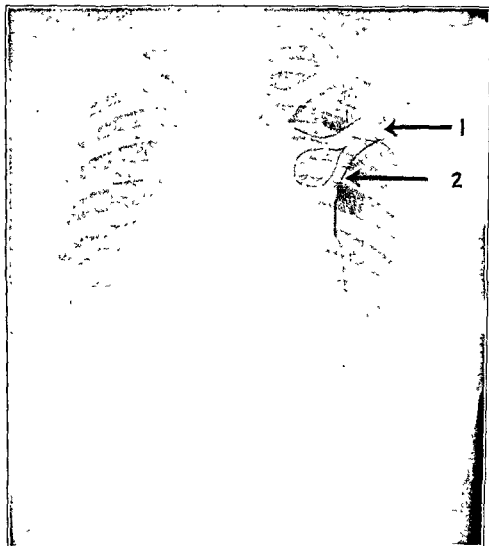


Fig 52.—Pneumothorax of four months' duration. Sputum quantity uninfluenced because of an uncollapsed cavity (2) held open by what proved to be a funnel adhesion (1) on thoracoscopic examination. The chest-wall attachment was electrocoagulated. (Retouched.)

spontaneously if the coagulation has been at the chest wall stump, but if the coagulation has been on the chest wall around the stump, one sees the adhesion gradually stretching out into a slender cord (Figs. 52 and 53). We have experienced unwavering success in securing a satisfactory collapse of cavities in cases presenting adhesions not suited for cutting.

Bleeding which occurs during the course of cutting, is also controlled by coagulation—either by allowing a stream of sparks to play from the tip of the electrode upon the bleeding area, or by clamping the vessel with the author's intrathoracic hemostat and switching on the coagulating current.

A highly damped type is the characteristic wave form of the coagulating current, and when this form is applied to the tissues, the heat produced within



Fig 53.—Same case as Fig. 52. One month after electrocoagulation. The adhesion is now a slender cord of no technical importance. Cough and expectoration absent.

the tissues can coagulate or veritably "cook" them, causing a shrinking of connective tissue. Blood-vessels are emptied and a collapse of their walls takes place, so there is no bleeding when they are cut through with the cutting current. As already cited, no cutting properties are comprised in the coagulation current, and its chief virtue is as a hemostatic agent; veins and arteries of a fair size may be readily sealed off, either before or after they are severed.

The power used and the length of time the current is applied regulate the extent of tissue coagulation in a given area. Should heavy power be employed and the current applied for but a brief interval, relatively superficial coagulation will be obtained; each type of tissue individualizes the amount of coagulation used. Undesirable charring and carbonizing of the tissue will result if current of high power is applied too long. In the case of coagulating a thick or dense adhesion, a weak current must be used for a prolonged period for the following reason: if a stronger current is applied, the tissue in the immediate vicinity of the electrode will promptly become dehydrated and even carbonized, forming such a defective conductor that the current will cease to flow—hence, the more deeply imbedded tissue will retain its former aspect.

It is advisable to expose adhesions that are thin to a strong current, but only for a short period of time so that the surrounding tissue will not be influenced. The use of the blunt electrode is most satisfactory when applying the



Fig. 54—Moderately damped wave, has excellent cutting qualities and gives a light degree of dehydration

coagulating current before cutting if more than a superficial layer of dehydration is needed. To do this, the current is turned on and the electrode drawn slowly in a line over the tissue of the proposed cutting. Any needed alteration of the current is made, observing the result through the thoracoscope, but over-heating is warned against—therefore, conscientious precaution must be practised to avoid any such oversight. Coagulation occurs with a strong current from 0.5 to 1 cm. in all directions from the electrode; but after a few days the zone of destroyed tissue cells extends beyond this area. This is a fact to be remembered, because damage to large blood-vessels and nerve trunks or other important structures is possible, giving rise to serious complications.

*Cutting.*—A continuous undamped wave high-frequency current, produced by radio-tubes, is a splendid cutting current, but it has very little, if any, dehydrating or coagulating effect upon severed tissue. Consequently, for intrathoracic use, it is not suitable because, as pointed out, hemostasis would prove a difficult problem, and, unlike open operations, the coagulating current would have to be resorted to constantly to control bleeding, as one cannot employ the usual methods of hemostasis—thus seriously handicapping the surgeon by delaying the operation.

For intrathoracic purposes, the best form of cutting current is one of extreme high-frequency and of wave form known as moderately damped (Fig. 54). By this type, an intense arc is engendered at the point of contact between the cutting electrode and the tissue. Tissues in the immediate path of this arc fall apart as if severed with a scalpel. One would suppose that the cutting is done by

the operating electrode, which is quite blunt, but it is really done by an electrical arc which forms ahead of the electrode, volatilizing the tissues as the current passes through the intervening space between the electrode and tissue. The intense heat generated at the point of contact also dehydrates the severed edges of tissue—the capillaries, lymph vessels and smaller blood-vessels are sealed off in this way and oozing is prevented.

While the degree of dehydration and electrocoagulation of the severed edges of tissue depends, to some extent, on the cutting surface of the operating electrode, the amount of power used, the depth of the cut and rate of speed with which the cutting electrode is moved, it depends chiefly on the character of the current or wave form. Furthermore, a greater or lesser degree of dehydration or coagulation may be produced upon the severed edges of tissue by varying the damping which a control lever regulates on the Bovie unit, causing at "light" setting a very thin dehydration of only a few thousandths of an inch deep; at the "heavy" setting, tissue may be coagulated on both sides of the severed edges to a depth of  $\frac{1}{32}$  to  $\frac{1}{16}$  of an inch. Therefore, a cutting current may be selected according to the vascularity of the tissue to be cut. The greater the blood-supply, the greater the degree of dehydration or coagulation which should be used.

While dehydration setting depends upon the vascularity of tissue, voltage must be regulated according to the character of the tissue to be cut. Low voltage is used generally; high voltage only when adhesions are dense and fibrous. The power control in cutting is also adjusted as the occasion requires. It is not necessary, in cutting adhesions, to do it rapidly, and deep incisions are certainly imprudent, so a weak current is most often used. To cut old, dense, fibrous adhesions more power is needed than in those composed of highly vascular, recently organized connective tissue. On the instant that it is required, an assistant must always be able to adjust the power controls and dehydration voltage. A weak power control setting is most practical and best for cutting adhesions. In practice, it is best not to apply more than a short portion (the tip, or only a few millimeters of the edge) of the operating electrode to the tissue to be cut. Should a larger portion be used, the cutting quality will be impaired. The tissue is not more than just touched by the operating electrode, preferably with the tip, and the action is that of following through the cleavage thus made. Absolutely all pressure and pulling, however slight, must be avoided. The sense of touch demanded by this procedure differs altogether from that of traction or pressure of surgical cutting, and a little practice is necessary to acquire it. One should not endeavor to make a deep cut with one stroke—it is much more advantageous to go over the same incision again, avoiding the already severed tissue.

### THE ELECTROSURGICAL TECHNIC.

Besides the electrosurgical unit, the following are the essential instruments for the electrosurgical method of severing adhesions: trocar and cannulas for introducing the operating electrode (already shown in Fig. 40), operating electrodes, extensions and operating tips for the electrodes.\*

\*Manufactured by Carl McKissick, 71 East 6th St., Portland, Oregon

**Operating Electrodes.**—Two operating electrodes are available—a flexible and a jointed one. Both of these electrodes are equipped with shaft extensions and three operating tips—one for coagulation, one for cutting, and one for deep puncture coagulation and cutting purposes. With exception of the distal half of its shaft (which is flexible) the flexible electrode (Fig. 55) is made of hard rubber. The shaft has a core consisting of two strips of metal, and is so constructed that by turning a knurled disk at the end of the handle, one strip of metal is shortened, thus bending the distal half of the shaft of the electrode. Any curve of the shaft up to  $45^{\circ}$  may be obtained by rotating its knurled disk.

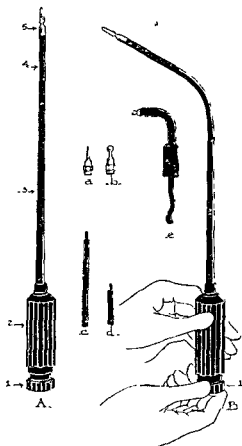


Fig. 55—Author's flexible electrode.

*A.* The instrument straight.

1. Knurled disk for flexing instrument.
2. Hand grip.
3. Hard rubber shaft except distal one-fourth which has a soft rubber covering
4. Medium shaft extension.
5. Operating tip.

*B.* The instrument flexed by turning disk (1).

- a.* Pointed tip for cutting and deep coagulation.
- b.* Coagulating tip.
- c.* Long shaft extension
- d.* Short shaft extension.
- e.* Connection with unit which fits in the shaft of the hand grip

The handle is hexagonal, whereby a firm grip with the fingers is assured. In introduction through the cannula into the pneumothorax cavity, no curvature is given the electrode (at least no more than slight) until under thoracoscopic view, when the desired flexure is obtained. The various curves of the shaft facilitate the approach to adhesions in various positions without the necessity of withdrawing the instrument and substituting another of a different curve. Because of this immediate convenience and adaptability, the device is extremely proficient.

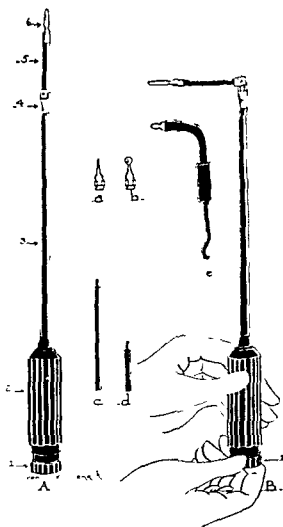


Fig. 56.—Author's jointed electrode.

- A The instrument straight.
1. Disk for angulating the instrument.
  2. Hand grip.
  3. Hard rubber shaft.
  4. Metal joint.
  5. Medium extension.
  6. Operating tip.
- B. The instrument angulated by turning the disk.
- a, b, c, d and e are the same as in Fig. 55.

The workmanship of the jointed electrode (Fig. 56) is very similar to that of the flexible electrode; but in it, the shaft is rigid, with a joint at the end. *Appropriate extensions may be inserted into the distal end of this joint.* By turning the knurled disk at the end of the handle, the distal end of the electrode may be directed at any angle up to 45°. Access to adhesions in any possible position is readily accomplished with this instrument, which is especially of value in approaching adhesions close to the chest wall puncture.

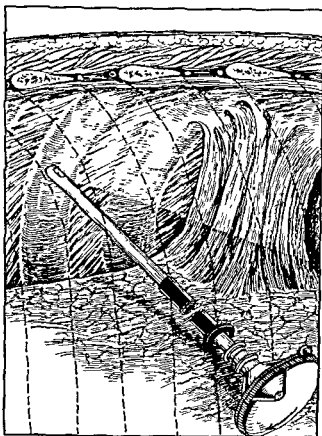


Fig. 57 —The thoracoscope, after having been introduced with the lens up, is rotated to bring the adhesion to be severed into view. The marker indicates the position of the adhesion at three o'clock.

The cable connecting the operating electrode with the electrosurgical unit is joined to the electrode by means of a right-angled, insulated, metal tip which fits into the handle of the electrode in such a way, that, while the electrode may be rotated, the cable does not turn with it, but always remains untwisted and out of the operator's way.

Operating tips of various patterns for cutting and coagulation are provided, as there are different surgical requirements to be met. These tips are screwed into the shaft of the electrode—also, if additional length is needed, three extension shafts are available.



The *modus operandi* of selecting a suitable site for introducing the operating electrode and placing its tip upon the adhesion to be cut is quite simple, if the method employed by the author since the beginning of his work, is followed, *viz.*, after having decided by thoracoscopy the adhesion to be severed and the point of severance, one notes by the indicator on the eyepiece of the thoracoscope, the direction the lens faces—for instance, the marker may correspond to three o'clock

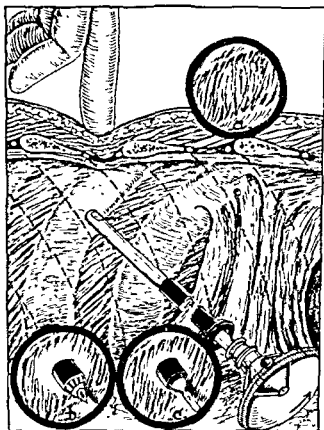


Fig. 58—The thoracoscope is now rotated anti-clockwise to find a suitable site for introducing the operative electrode (the marker indication twelve o'clock). The inner chest wall area is located on the outer chest wall by palpation with the finger, producing a bulge of the intercostal space when seen through the thoracoscope (a). (b) Thoracoscopic view of trocar and cannula entering the pneumothorax cavity (c) Trocar has been removed and tip of operative electrode is seen emerging from the cannula.

(Fig. 57). The thoracoscope is then rotated anti-clockwise until the intercostal spaces come into view (say twelve o'clock) (Fig. 58). While still viewing the inner chest wall through the thoracoscope, one palpates the outer chest wall, corresponding to that seen through the thoracoscope, with the index finger. As pressure is made with the finger, the intercostal space will be seen to bulge (Fig. 58 a). The unerring precision of this method renders it of inestimable value in determining the point of puncture of the cutting instrument. If the area is appropriate, from the standpoint of surgical anatomy, one anesthetizes the place for introduction of the electrode in the same manner as for the thoraco-

scope; the infiltrating needle, however, is passed into the pneumothorax cavity and observed through the thoracoscope. Under thoracoscopic direction, the needle is then removed enough to allow careful infiltration of the pleura and endothoracic fascia; this portion will appear elevated and blanched through the thoracoscope. A small skin incision is made and the trocar and cannula for the operating electrode are gently pushed through the chest wall and viewed through the thoracoscope.

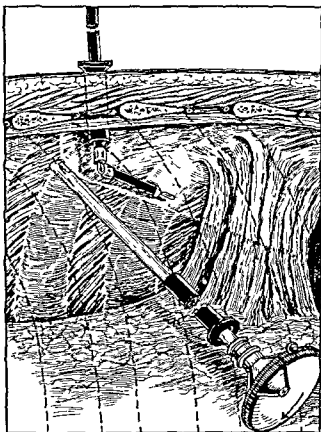


Fig. 59.—Keeping the tip of the electrode in view, the thoracoscope is rotated clockwise. The electrode is here seen pointing toward the under side of the adhesion—it must be straightened sufficiently to pass the adhesion and rotated forward.

The trocar and cannula for the operating instrument is passed through the chest wall in the same manner as for the thoracoscope, except that its entry is directed by thoracoscopic guidance in order that the trocar enters the pneumothorax cavity through the center of the blanched area in the intercostal space (Fig. 58 *b*). While still viewing this area through the thoracoscope, the trocar is withdrawn and the operating electrode inserted cautiously. One observes the tip coming into view (Fig. 58 *c*), and while introducing the electrode slowly, the thoracoscope is rotated clockwise back to the position of three o'clock, keeping the tip of the electrode constantly in the field of vision (Fig. 59). When the adhesion comes into view the operating instrument will be in position to apply it to the tissue to be severed (Fig. 60).

Before proceeding to cut, the tip of the instrument is first placed upon the adhesion, which is tested for sensation. This maneuver gives valuable data as to whether or not the adhesion is covered with pleura reflected from the lung or chest wall—as only the latter has sensory nerve fibers. The adhesion may be lifted with the blunt electrode tip and examined beneath for blood-vessels and lung tissue. Decision as to the point where the adhesion is best cut will depend upon its type and its relationship to important structures and nerve trunks, as well as the pericardium.

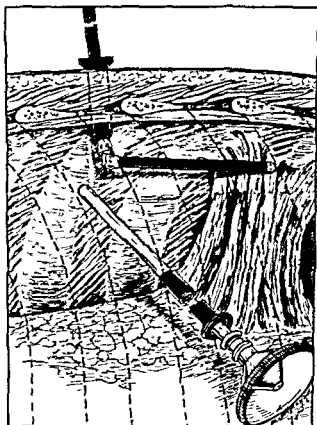


Fig. 60—The electrode is again angulated and rotated downward in position to cut.

In proceeding to sever the adhesion, I reiterate that the closer the cutting is to the chest wall, the greater will be the pain and the danger of bleeding, inasmuch as sensation comes from the intercostal nerves, and the blood supply of adhesions is derived, mostly collateral, from the intercostal vessels. Apical adhesions may derive a collateral blood supply from the thyrocervical trunk. Division near the lung, while painless, is dangerous, as opening may be made into a prolongation of a cavity projecting within the adhesion, or into compressed lung tissue: should either of these occur, a spontaneous pneumothorax, or liberation of infection, would predict an empyema almost certainly. In spite of all disputation voiced by others, one ought to adhere quite uniformly to the rule of always dividing the adhesion close to the chest wall. Naturally, an occasional

instance will be met with where this rule will not apply, as in the case of fan adhesions, but it is the most reliable guide to those lacking in experience.

*Multiple Adhesions.*—If multiple adhesions are present, suitable for cutting, one must select a site for introducing the electrode which will afford appropriate approach to all needing cutting. However, the same technic is followed, with due consideration of their position, which one notes by the marker on the thoracoscope. One must under no circumstances (in spite of feeling positive that the position of the adhesion is so well known that it is unnecessary to keep the tip of the electrode constantly in view) attempt to place the electrode upon the adhesion unless viewed directly through the thoracoscope. Should the blind method be yielded to, one may thrust the operating instrument into the lung or other structure, perhaps doing great, at least unnecessary damage.

After one adhesion has been severed and others remain to be cut, and if their position is known with relation to the first one, one still keeps the tip of the operating instrument in view and rotates the thoracoscope so as to bring them into the field of vision. I must emphasize the fact that the tip of the operating instrument must be constantly in view. If, by accident, it passes out of the field of vision, do not attempt to place it in sight by moving it, but rotate the thoracoscope. If not at once successful in locating the tip of the electrode, withdraw the latter well up into the cannula and begin all over again.

The beginner must limit himself unconditionally to string, cord and small band adhesions; the spindle, funnel and diffuse fold types must be excluded completely. Also no tissue must ever be cut until all surfaces have been seen, and *no tissue should be severed until the operator is perfectly familiar with its structure*; this rule is to be regarded inviolable, and by following it rigidly, accidents will be avoided.

Upon complete severance of the adhesion, a careful examination should be made: first, of the chest wall stump for bleeding vessels, and then of the lung stump. If blood is oozing, it should be stanchied by application of the coagulating current. Bleeding from the chest wall stump is much more probable than from the lung stump, as it will be seen that the lung stump contracts after cutting. Other adhesions requiring cutting are dealt with in a similar manner. Final affirmation that all bleeding from the stumps of severed adhesions is positively curbed must be done without oversight—the points where the instruments were introduced must be given the same consideration. If a fair amount of blood is present, it should be aspirated.

After the operator has assured himself that nothing is amiss within the pneumothorax cavity, the operating electrode and cannula are withdrawn and the site once more examined through the thoracoscope for bleeding from the puncture on the inner chest wall. The thoracoscope and cannula are withdrawn if no bleeding is present.

All coughing by the patient is prohibited. A small roll of one-inch gauze bandage for compression is held firmly over the site of the puncture. This is covered with sterile gauze, and the chest securely bound with strips of three-inch adhesive plaster, extending well to the front and back.

### JACOBÆUS-UNVERRICHT METHOD OF SEVERING ADHESIONS.

In this method, the galvanocautery is used for cutting purposes. There are two sets of instruments commonly employed for galvanocauterization—those of Jacobæus and those of Unverricht: the latter are generally used in this country. The Unverricht instruments necessary for galvanocauterization, except a transformer for regulating the heat of the cautery and the Unverricht thoracoscope (already shown in Fig. 39), are shown in Fig. 61. The technic of operation is the same as that described in the author's method, with such changes as apply

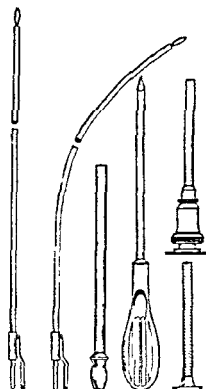


Fig. 61—Unverricht's instruments for galvanocauterization of adhesions (except the thoracoscope which is shown in Fig. 39).

Left to right: Straight cautery, curved cautery, smoke cannula, trocar for ball valve cannula, flexible cannula for the cauteries and (above) ball valve cannula for the thoracoscope.

to the use of the different cutting instruments; then too, the entirely different kind of electrical energy requires a technic in cutting the adhesions which is quite unlike that when a high-frequency current is used. The technic of thoracoscopy—whether one uses either the Jacobæus or Unverricht instruments for burning adhesions—is identical with that described in the author's method, except that with the Unverricht instruments no advantage is gained by using the author's bakelite cannula for introducing the thoracoscope, if it is utilized with hopes of interchanging the thoracoscope and galvanocauteries as one can the Unverricht thoracoscope and the author's electrodes.

Accordingly, unless additional punctures are made or the Jacobaeus instruments utilized, a study of the adhesions must be confined to one point and operation performed through the other site.

The Jacobaeus instruments (Fig. 62) comprise a *thoracoscope* and *two cannulas* of equal size—one each for the thoracoscope and cautery. The thoracoscope is considerably smaller than the Unverricht and gives a smaller image. The cannulas, being straight, offer an interchange of instruments, but only a

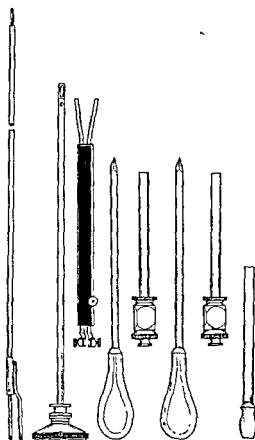


Fig. 62.—Jacobaeus instruments for galvanocauterization of adhesions.

Left to right: Straight cautery, thoracoscope, handle for cautery, two trocars and cannulas of the same size for thoracoscope or cautery, smoke cannula.

straight shaft cautery can be used which renders approach to some types of adhesions difficult.

The Unverricht thoracoscope is introduced into the pneumothorax cavity by means of a ball-valve cannula. We consider a cannula of this type disadvantageous because the intrapleural pressure remains the same as it was prior to the introduction of the thoracoscope. When the trocar is removed from the spiral cannula, before the introduction of the cautery, the inflow and outflow of air often changes the character of the pneumothorax as well as the position of adhesions. Consequently, any study of adhesions and conclusions as to the operative approach made before the changes in the intrathoracic pressure can be con-

siderably altered. (It is a distinct advantage to be able to study adhesions as they will be found when the operator is ready to cut them; this obtains in the author's method, using a valveless lakelite cannula, acceptable for either the thoracoscope or operating instrument—and, as stated, one can then study adhesions or operate from two points which is sometimes desirable.) While Unverricht's spiral cannula, through which the cautery is introduced, provides facilities for using either a straight or curved cautery, at the same time it proves a troublesome instrument, since frequently the shaft of the cautery becomes sufficiently hot to cause the tissues of the chest wall to stick to the cannula; when an effort is made to remove it after the operation has been completed, the coils of the spiral separate, thus engaging tissue which makes its removal difficult. If it is adherent and too much pull is resorted to, the spiral only spreads and may possibly break, which is exasperating; the portion left within the chest wall must be exposed, leaving a much larger chest wall wound than desirable. Yet another disadvantage of the Unverricht instruments is that they are not interchangeable. One cannot introduce the thoracoscope through the spiral cannula for the cautery. Should the Jacobaeus thoracoscope be changed to provide a field of vision equal to the Unverricht instrument, we would recommend his outfit as far superior to Unverricht's, for use in the galvanocautery method of operation. Unfortunately, the Unverricht thoracoscope is too large to pass through the Jacobaeus cannulas, so utilization of it with the latter instruments is impossible. When the author employed the galvanocautery method, after extensive experience with both the Jacobaeus and Unverricht instruments, the Unverricht instruments were chosen solely because the thoracoscope was better and it was felt that the disadvantages of the other instruments were somewhat overcome by the superior vision offered by the Unverricht thoracoscope.

*Technic.*—Matters of technic differing from the author's when the galvanocautery is used, follow: I have already stated that severing adhesions is best performed in a dark surgery because the vision is improved. Therefore, before introducing the galvanocautery, the operating room must be darkened and the cautery brought to a dull red glow. In a lighted operating room this degree of heat will not show any change of color on the cautery tip, which accounts for "cold cautery" recommendations by those who utilize the galvanocautery without an absolutely light-proof operating room. After the heat of the cautery has been adjusted, the current is switched off and the cautery allowed to cool. It is then introduced into the cannula and the operating room darkened. The same technic of placing the cautery upon the adhesion to be cut is followed as described in using the author's instruments. After the cautery is properly placed close to the tissue to be burned, the current is turned on, and after the required time to heat the cautery to the proper glow has elapsed, one places the cautery tip upon the tissue. Cauterization should proceed slowly and cautiously by repeated short strokes. Only short strokes should be made and the cautery removed from the tissue before it has become cooled, otherwise it will stick and when pulled away may result in a tear. If the cautery becomes attached to the tissue, the heat should be increased until it is free, and only gentle traction used—an attempt to pull it away must under no circumstances be made. If blood

channels are visualized, they should be obliterated by placing the flat surface of the cautery upon them for a few seconds. The operator proceeds with the cauterization as has been directed. Should bleeding occur, it may be stopped by applying the heated cautery, but if unsuccessful, one should resort to radiating heat from the tip of the cautery held a few millimeters away from the bleeding vessel.

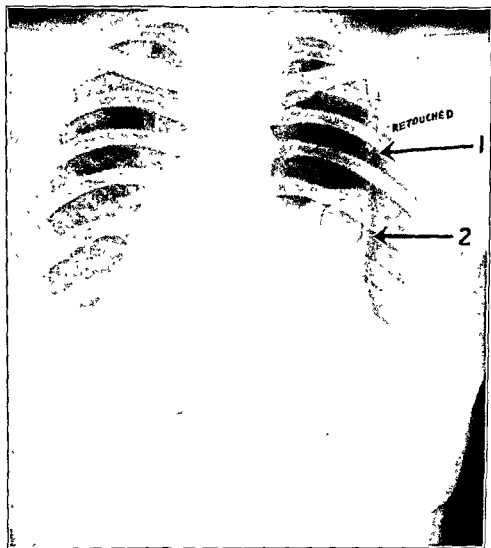


Fig. 63.—(Retouched.) Long cord adhesion (1) preventing closure of cavity (2) in pneumothorax of four and one-half months' duration. Temperature 100°-101° F. in P. M. Sputum tubercle bacilli positive.

The tip of the cautery must always be in full view, and the thoracoscope is rotated, if necessary, to make sure the shaft of the cautery is not resting upon the lung or other important structures, which might be damaged by its heat. Inspection of the heat in the shaft of the cautery from time to time must not be neglected, as damage can occur to the chest wall, resulting in a pleuro-cutaneous fistula.



Prolonged cauterization is undesirable because of reaction caused by chemical changes which tissue proteins undergo at the site of cauterization. The operation should be conducted by repeated heating and cooling of the cautery. From our studies on exudate formation, we are convinced that prolonged use of the heated cautery is an important factor in postoperative exudate formation and pain



Fig. 64.—Same case as Fig. 63 Forty-eight hours after operation, showing uncollapsed thick wall cavity (1). (Retouched.)

Attention is directed to the danger of utilizing a heated cautery in close proximity to large blood-vessels and important nerve trunks, as the former might result in phlebitis or vascular thrombosis, and the latter in painful neuritis. In attempts to sever adhesions in the costovertebral gutter, serious complications may arise from application of a cautery too close to the sympathetic trunk.

The cauterization of large adhesions of the band and spindle type may be tedious and tempt the operator to increase the heat of the cautery so that faster

cutting may be executed. However, many delays will be occasioned by smoke interfering with vision, requiring replacement of the cautery with the smoke cannula. Smoke removal may be hastened by instructing the patient to clear the throat or take a few deep breaths.



Fig. 65—Same case as Fig. 64. Three months after operation. Positive pressure was necessary to collapse the cavity. No cough or expectoration. Three years later patient clinically well.

After the adhesions have been severed, the same study should be made for bleeding of the chest wall and lung stumps, as well as the chest wall punctures, as already described in the electrosurgical method. The same postoperative care is applied when the Jacobaeus method is used as that outlined in the author's method. Objections to the galvanocautery method have already been stated.

## POSTOPERATIVE CARE.

The patient is placed in bed with the pneumothorax side up (or the side which has been operated on) for the first twenty-four hours, and absolute bed rest continued for a minimum of seven days. If there is any coughing, it can be controlled with codein, dionin or even morphine (if necessary), during the first twenty-four to forty-eight hours. The patient must be instructed on the

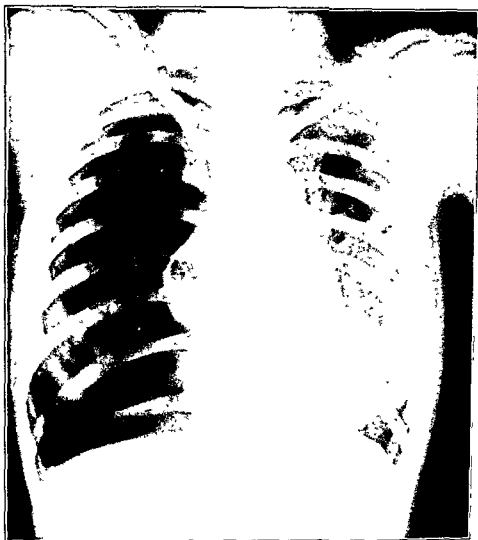


Fig. 66.—Cavity drainage blocked four days after operation in a case wherein a large band adhesion had been severed and the first refill was too large.

necessity of abstaining from all exertion—straining at stool and physical effort, including sneezing and excessive laughter.

The strictness and duration of the postoperative care, before the case reverts back to the medical service for continuance of pneumothorax treatment, depends upon the character of the operation and the patient's reaction. Usually the postoperative course is not rigorous; it is especially bland following electrosurgical

cutting, a temperature of 99° to 100° F. may sometimes last only a few days. Postoperative pain, if any, is very trivial and easily relieved with codem.

A roentgen film should be made after twenty-four to forty-eight hours, and the time and quantity of gas reinflation decided upon. As a general rule, the intrapleural pressure will be less than before operation. Positive pressures should be avoided, if possible; but, if thick-walled cavities are present with

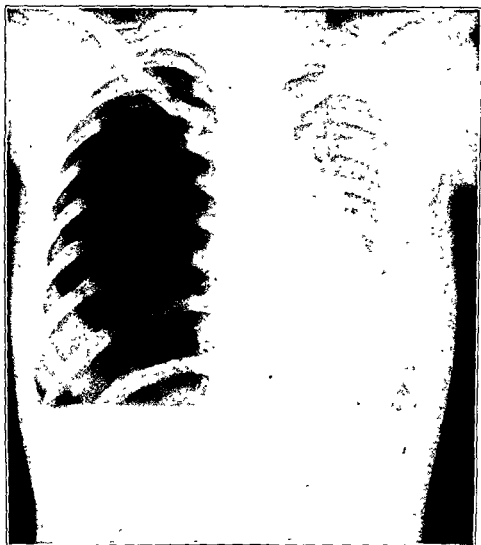


Fig. 67—Same case as Fig. 66. Fifteen days later following aspiration of air and smaller refills, establishing a gradual collapse of the lung. Cavity now completely closed.

thickened pleura, it may be necessary to resort to positive pressures to secure closure of offending cavities (Figs. 63, 64, 65). If there is interference with cavity drainage and retention of sputum, aspiration of air and slight expansion of the lung may be necessary to institute drainage, following which, frequent refills with smaller quantities of air should be carried out until a satisfactory collapse is established, and the patient rendered free of sputum (Figs. 66 and 67).

Reinflation is carefully controlled by the roentgen-rays, and, for the first few inflations, a roentgenogram should be made, *preferably after every air injection*.

In one or two weeks (with the exception of complications), the sanatorium patient may return to the preoperative routine. Individualization will be made *regarding the routine of ambulant and working patients admitted for operation*.

It is a general rule that after adhesions have been cut, pneumothorax refills will be required less frequently than before. This may be due to the mild pleuritic reactions causing some pleural thickening with consequent less rapid absorption of gas.

### COMPLICATIONS.

The complications after operation, in our series of 249 cases, are shown in Table II. It will be observed that the commonest complication is exudate forma-

TABLE II\*  
COMPLICATIONS AFTER OPERATION INCLUDING THE GALVANOCAUTERY  
AND AUTHOR'S METHOD  
249 Cases

Serous exudate	63—25.7 Per Cent.
Purulent exudate	41—16.5 Per Cent.
Hemorrhagic exudate	26—10.4 Per Cent.
Febrile reaction	7—2.4 Per Cent.
Severe hemorrhage	3—1.2 Per Cent.
Bronchopleural fistula	4—1.6 Per Cent.
Spontaneous pneumothorax	1—0.4 Per Cent.
Severe postoperative vomiting	1—0.4 Per Cent.
Gas embolism	0
Shock	0
Severe surgical emphysema	0

\*This table comprises complications occurring in 136 cases operated upon with the galvanocautery and 113 cases operated upon by the author's method. However, in 35 of the latter group, an obsolete high-frequency apparatus was used, while in 78 cases the Bovie unit was employed.

tion. This sequela follows essentially the same evolution as observed during the course of pneumothorax therapy, as previously discussed. A small quantity of exudate in the phrenicocostal sinus may be detected roentgenologically in the vast majority of cases following operation by the galvanocautery method, but much less frequently after the electrosurgical method. This is also true regarding other complications. If an extensive operation is done with the galvanocautery, one may expect fever, usually chest pain and exudate formation. When utilizing the electrosurgical method, very extensive operations may be performed, frequently with no reaction aside from a small amount of exudate accompanied by a slight elevation of temperature lasting two or three days.

In our 249 operated cases, Group A, comprising 101 cases, had no exudate either before or after operation. Group B, 64 cases, had no exudate before operation but developed it afterwards. Group C, 84 cases, had exudate both before and after operation. Of the 64 cases in Group B, who had no exudate before operation, 50 developed serous exudate after operation, and in 20, it disappeared by absorption, as the quantity was not sufficient to justify aspiration. In a like number (20), it disappeared after aspiration, and in 14 it became purulent. In this same group (B) 14 cases developed hemorrhagic exudate, 8 became serous

and 6 became purulent. In many instances of exudate formation of the serous and purulent type, there was a lapse of many months before it appeared. Nevertheless, they have been included as postoperative, although it is safe to say the vast majority would have had exudate without operation, as caseating tubercles were seen both upon the visceral and parietal pleuræ at the time of operation. The hemorrhagic exudates were noted within twenty-four hours after operation and were directly attributable to the operation. The cases were almost entirely those operated upon by the galvanocautery or by an unnamed high-frequency machine of the tube type, delivering a cutting current without dehydration properties. Since adopting the Bovie unit, hemorrhagic exudate has occurred only once. This case had to deal with a high-strung youth with band adhesions consisting of many vascular areas. The adhesions were in the pleural cupola

TABLE III  
COMPARATIVE FREQUENCY OF EXUDATE FORMATION  
FOLLOWING VARIOUS OPERATIVE METHODS  
*249 Cases*

	Jacobaeus Method	Author's Method	
	Galvanocautery 136 Cases	Unnamed High Frequency Unit 35 Cases	Bovie High Frequency Unit 78 Cases
Serous exudate	28—20.5%	11—31.4%	3—3.8%
Purulent exudate	36—26.4%	4—11.4%	2—2.5%
Hemorrhagic exudate	14—10.3%	11—31.4%	1—1.2%

and close to the brachial plexus. Attempts to coagulate before cutting induced painful muscle reflexes which alarmed the patient, and the operation was therefore executed without previous coagulation. A small amount of bleeding, possibly 50 c.c., took place.

It is noteworthy that no purulent exudate was due to exogenous infection; all were tuberculous and were attributed mostly to the independent evolution of disease; a few were known to be caused by cutting into tuberculous foci encountered within adhesions of the fold, diffuse and spindle type. Every purulent exudate was predicted at the time of operation. With improved instruments and technic, we are certain our incidence of exudate formation will be lowered even much more.

It should be pointed out that the first 136 cases were done with the galvanocautery, and of the remaining 113 cases, 35 were performed with an unnamed high-frequency machine which provided a cutting current, but possessed no dehydration qualities; whereas, the last 78 cases were operated with the Bovie unit.\*

Table III shows the incidence of exudate formation following use of the galvanocautery and two types of high-frequency apparatus. In our work, we first

\*In the above cases, not only the large model unit but also the less expensive portable unit were used—both were entirely satisfactory. However, numerous other models were tried on these cases and proved unsatisfactory; the operation was therefore completed with the Bovie model.

utilized the galvanocautery, but because of the objections already given, we turned to the high-frequency current and used a model which delivered a cutting current devoid of dehydration properties, which, while rendering better service than the galvanocautery, was objectionable because of the difficulty of controlling bleeding. We then adopted the Bovie model, and it will be noted that the incidence of all types of exudate has been materially reduced. Admittedly, greater experience has also been a factor, together with selection of cases and better operative judgment and technique.

Consequently, the frequency with which serous, purulent and hemorrhagic exudate may be expected to occur cannot be estimated by Table II. Quite a different version regarding the above complications is revealed in Table III. When one studies the results of the different types of cutting methods used by the author, one can appreciate the value of the advantages of the Bovie high-frequency unit for this special kind of surgery. Admittedly, experience has also contributed materially to the lowered frequency of complications.

*Postoperative exudate* follows essentially the same evolution as observed during the course of pneumothorax therapy, as previously discussed. A mild pleuritic reaction takes place in the majority of cases where the pneumothorax is of recent issue (under three months), and a small amount of fluid will be found fluoroscopically in the phrenicocostal sinus, if the galvanocautery is used. By the author's method, exudate will occur infinitely less frequently.

It should be mentioned that of the three instances of severe hemorrhage, one occurred during use of the galvanocautery and two during operation with the unnamed high-frequency machine. The single case of spontaneous pneumothorax occurred on the contralateral side seven days after operation; it was due to an asthmatic paroxysm and was fatal. This case represents the only fatality in the entire series, directly or indirectly due to operation.

*High Fever.*—This complication was seen only after use of the galvanocautery in seven cases, when, twenty-four hours postoperative, the afternoon temperature ranged from 100° to 103° F. and was followed by acute exudate formation. Each case had to deal with extensive operations. In five cases the temperature, within two weeks, came to normal after aspiration but it lasted several weeks in two instances and the exudate became purulent. One made a complete recovery following aspiration; the other, after repeated aspirations, required tube drainage and, eventually, a complete posterior and anterolateral thoracoplasty followed by an undocking operation. The patient made a complete recovery.

*Bronchopleural Fistula*—Bronchopleural fistula was definitely present in four cases—however, only two were directly or indirectly related to the operation. One case had to deal with a funnel adhesion which was cut at the chest wall, but lung pigment was encountered in scattered areas (Fig. 68). Because of tuberculous changes in the visceral and parietal pleura, oleothorax treatment was begun, and one month later the patient expectorated the oil. The fistula finally healed and the patient now has a satisfactory oleothorax, free of purulent exudate.

The second case attributed to the operation was one wherein four operations had been performed to sever numerous adhesions. The fifth operation was for

the purpose of severing a spindle adhesion. The operation was technically successful, but owing to a caseous pleuritis, the patient had been treated with oleothorax, the oil being recovered each time before operation. After the last operation, the oleothorax treatment was resumed, and two weeks later oil was expectorated, which occurred, at times, during a period of the next six weeks, when the fistula healed.

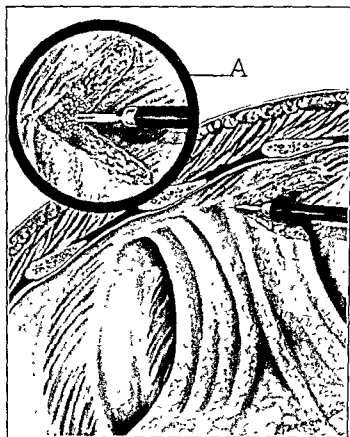


Fig. 68—Partially severed spindle adhesion containing compressed lung tissue—showing operating electrode in position over the cut near the chest-wall attachment of the adhesion.

*A.* Close-up view of the apex of the cut showing fine air bubbles indicating the cut has extended into lung tissue. This type of adhesion should be electrocoagulated at its chest-wall attachment and not cut.

The other two cases were unquestionably due to the independent evolution of the underlying tuberculous process, as both occurred more than six months after operation.

*Severe Postoperative Vomiting.*—This isolated case was due to a morphine idiosyncrasy. There was no instance of shock, severe emphysema or severe postoperative pain.

*Hemorrhage During Operation.*—The usual source of bleeding during the process of cutting adhesions is from blood-vessels collateral from the intercostals. One meets with two types of vessels: those situated subpleurally, which



can usually be detected by thoracoscopic examination and easily controlled, and those situated in the interior of adhesions, from which profuse bleeding occurs at times. In the case of the former, bleeding may be easily controlled by electro-coagulation; or, if the galvanocautery is used before the blood-vessels are cut, they may be thrombosed by the application of the flat surface of the cautery. Dangerous bleeding, however, comes from blood-vessels situated in the interior of adhesions, particularly in those which are dense and well organized. This compressed type of adhesion is found in cases in which the patients have been subjected to prolonged (sometimes even short) periods of pneumothorax treatment, particularly if the patient is of a fibroplastic constitution with a tendency for productive changes to take place in the tissues following pneumothorax treatment.

The latter type of vascular adhesion is more often found in the costovertebral gutter, at the apex of the lung and anteriorly near the costochondral junction (see Case 2). Densely organized adhesions in these areas should be approached cautiously because blood-vessels of considerable size may be situated in their interior, the presence of which is not always possible to determine until they have been cut into.

Bleeding occurring during the cutting of cord and band adhesions, if the adhesions are not densely organized, usually desists after the adhesion has been cut through and the stump contracts. In well organized tissue, however, little retraction takes place, and bleeding may be a source of much concern to the surgeon. Therefore, it is obvious that the ideal method of severing adhesions is one that will provide efficient hemostasis.

Profuse hemorrhage during operation is perhaps the most feared complication in executing the closed intrapleural pneumolysis. Certainly, the three occurring in the author's experience have left a never-to-be-forgotten impression. All three were controlled and the patients made uneventful recoveries. One occurred during utilization of the galvanocautery, and two occurred when we first adopted the electrosurgical method, employing a high-frequency machine which delivered a cutting current lacking in coagulating properties. The details of the three cases follow:

CASE I.—The first case was encountered early in our experience. It occurred during a clinical demonstration of the cutting of adhesions with the galvanocautery, according to the method of Jacobaeus-Unverricht. The patient was unfit for such a demonstration, as the operation was difficult, owing to the many adhesions to be cut. By permitting others to view the work through the thoracoscope, these frequent interruptions markedly delayed the operation, which was being done cautiously with only a minimum heat in the cautery because of vascular adhesions. The patient's state of mind, as a result of conversation, made it necessary to speed up the work, whereupon the heat in the cautery was increased to a moderate cherry-red glow. All went well for a short time, when suddenly a gush of blood smeared the lens entirely, obstructing the view. The thoracoscope was quickly withdrawn and wiped clean, but on reintroduction, the lens at once again became covered with blood. Knowing the exact site of the bleeding vessel, we were able to alter the patient's position on the table

so that blood no longer fouled the lens and the bleeding vessel could be clearly seen. The hemorrhage was eventually controlled by cauterizing tissue immediately surrounding the vessel and also by touching the vessel itself with the tip of the cautery. Two liters of blood were aspirated from the pneumothorax three days later. The patient suffered no inconvenience as a result of the accident, but the formidable experience is yet so vivid in the mind of the author that he is convinced this type of operation is not appropriate for clinical demonstration to groups. Demonstrations should be confined to a very selected, interested few.

The two other hemorrhages which occurred in our series, while profuse for a moment, were easily controlled by electrocoagulation.

CASE 2 (6557).—In CASE 6557, a woman aged 25, referred for pneumolysis, had been under pneumothorax treatment for 9 months. Stereoscopic films showed an uncollapsed cavity in the upper lobe of the right lung suspended by a cord adhesion attached to the anterior end of the third rib and by two strings and one band adhesion attached between the second and fourth ribs posteriorly in the costovertebral gutter.

Thoracoscopic examination confirmed these observations. The posterior adhesions were cut with the operating electrode after electrocoagulation and without anything unusual happening, as was expected. The cord adhesion anteriorly was then carefully studied. It was round, approximately 1 cm. in diameter (a minor affair from the standpoint of size alone). No blood-vessels were visible on its surface. It was densely organized and sensitive up to 3 cm. from the chest wall, when all sensation disappeared. On slight coughing or clearing of the throat on the part of the patient, the adhesion increased in diameter up to approximately 4 cm. from the chest wall, suggesting that it contained either the prolongation of a cavity or lung tissue, the former being suggested by previous stereoscopic film study. Pulsation of an expanding type was noted at the attachment of the adhesion to the chest wall, but not beyond 1 cm. from the chest wall. The pulsation was synchronous with the cardiac systole and not transmitted from the moving lung. A zone of electrocoagulation was made around the adhesion 2.5 cm. from the chest wall so as to avoid lung tissue and get as far away as possible from the chest wall.

On cutting, the adhesion proved to be very fibrous. Little contraction of the cut surface took place. Small blood channels were encountered as the severing continued, which was always preceded by electrocoagulation. Suddenly, near the center of the adhesion, a blood-vessel that had not been obliterated by the electrocoagulation, was cut into—no doubt because of the density of the tissue and because the electrocoagulation current was not sufficiently intense. A stream of blood was projected across the pneumothorax cavity to the lateral thoracic wall. The lens, fortunately, was so placed that it did not become smeared with blood. The author's blunt electrode was placed on the bleeding vessel, but electrocoagulation at this point only made matters worse, as the bleeding became more profuse, whereupon the pointed electrode was introduced into the tissue close to the wall of the vessel and the coagulating current increased for depth; this controlled bleeding immediately. The adhesion was cut through

without further loss of blood. No unfavorable result from the bleeding was suffered by the patient. Two hundred and fifty cubic centimeters of blood were aspirated from the pneumothorax the following day. The operation was a complete clinical success.

I am certain that the hemorrhage in this case would have reached serious proportions if we had been obliged to rely on the galvanocautery for control. As a matter of fact, I do not think we would have attempted cutting this adhesion with a galvanocautery.

CASE 3 (6500).—In the third case, No. 6500, a woman aged 24, referred for pneumolysis, had been under pneumothorax treatment for ten months. At first, the quantity of sputum became diminished and then remained stationary, averaging from 40 to 60 c.c. in twenty-four hours during the last two months of pneumothorax treatment, when she developed tuberculosis of the larynx and extension of disease to the opposite lung.

Stereoscopic films showed a large cavity in the upper lobe of the left lung. There were many band and cord adhesions attached posteriorly in the costo-vertebral gutter and to the dome of the pneumothorax cavity above the first rib. Several cord and band adhesions were attached to the anterior end of the first, second and fourth ribs.

Thorascopic examination revealed that all of the adhesions were densely organized and contained numerous subpleural blood-vessels. At the first operation, a large band adhesion attached to the anterior end of the fourth rib, as well as a band adhesion holding the lung to the aorta, and two string adhesions at the apex were cut. One of the latter was attached to the wall of the subclavian artery, while the other was attached 4 mm. from the vessel. No bleeding occurred, hemostasis being perfectly controlled by electrocoagulation, and no reaction followed the operation.

At the second operation, two large band adhesions, one attached to the first intercostal space and the second to the third rib in the costovertebral gutter, were cut, again without bleeding or unfavorable complications.

At the third operation, two dense cord adhesions attached to the anterior end of the first and second ribs were cut. All of these operations were technically difficult, but bleeding was perfectly controlled by electrocoagulation, which alternated with the cutting. Following the operations, each of which was done at intervals of two weeks, an improved collapse of the lung was noted on stereoscopic films after each operation. The quantity of the patient's sputum was gradually reduced to 15 c.c. as shown by daily measurement.

At the time of the previous operations, thorascopic study of the remaining adhesion showed that it was attached to the dome of the pneumothorax approximately 1 cm. distant from the subclavian artery just before this vessel crossed over the first rib. Furthermore, collateral blood supply was seen emerging from beneath the subclavian artery and entering the base of the adhesion near its center. This collateral blood supply probably came from the *arteria cervicalis profunda*, which in this case may have been a branch of the subclavian artery instead of the costocervical trunk. The adhesion was admittedly of a dangerous type, one we would not have considered cutting with the galvanocautery. Our

success with electrosurgery, however, encouraged me to attempt it by the latter method, as the quantity of the patient's sputum had remained stationary at 15 c.c. daily, and both stereoscopic film study and thoracoscopic study showed the remaining adhesion to be of great technical importance. Undoubtedly a satisfactory collapse of the lung (on which the patient's recovery depended) would not be obtained until it was severed.

The band was therefore carefully electrocoagulated on its outer surface, but because of its position, it was impossible to study its inner surface or put an electrode in a position to do an electrocoagulation of that surface. A line of electrocoagulation was made 2 cm. from the chest wall on the outer surface, and cutting followed with the undamped current, of moderate intensity, first, from the posterior edge toward the center and then from the anterior edge toward the center. As the center of the adhesion was approached from either side, the band was found to be more and more densely organized with tough bands of fibrous tissue between which were numerous blood channels. Because of the dense character of the tissue, little retraction of the cut surface took place, and it was constantly necessary to resort to the coagulating current to control bleeding. On further approaching the site of the collateral blood supply, after cutting through a particularly dense band of fibrous tissue, a sudden profuse hemorrhage took place. For a time it seemed uncontrollable, and preparations were made for blood transfusion and thoracotomy for the purpose of placing a clamp directly on the bleeding vessel. Fortunately, just at the moment when failure to control bleeding seemed imminent and no further time was to be wasted by attempting to control it with electrocoagulation currents, the method of puncturing around the blood-vessel and doing a deep coagulation proved successful, and all bleeding stopped. It seemed reasonably certain that the vessel had not been severed but only cut into, and that the remaining portion of adhesion contained other blood-vessels of a dangerous size. Lack of confidence in being able to control bleeding prompted us not to attempt further operation, at least until some more certain method of hemostasis could be developed.

The patient suffered no unfavorable symptoms as a result of the hemorrhage, except a slight febrile reaction which lasted three days. The pneumothorax cavity was filled with carbon dioxide gas, and the intrapleural pressure was considerably increased over former inflations. Forty-eight hours after operation, 400 c.c. of bloody exudate was aspirated.

The quantity of the patient's sputum remained unchanged by the operation, as was expected, and for four weeks following operation, the daily quantity of sputum remained 15 c.c. Anticipating such a course and convinced that a method must be found for cutting the offending band without danger of hemorrhage, I devised an intrathoracic hemostat (Fig. 69). After the instrument was tested with satisfactory results, the final operation was decided on.

The thoracoscope was introduced in the first intercostal space midclavicular line. A superb view of the remaining uncut band was seen. The collateral blood supply was seen as on previous examination. The adhesion had every indication of extreme vascularity. There was no necrosis at the site of previous cutting, and the cut surface was clean. The intrathoracic hemostat was introduced

While it is reported in the literature that the phrenic nerve sometimes passes through the subclavian vein, we have never seen it, but we can confirm Goetze's observations regarding the intimacy between the associate phrenic and the vein. In one instance, Plenk and Matson in their cadaver dissections, found the associate phrenic passing through the wall of the subclavian vein. An exaïresis

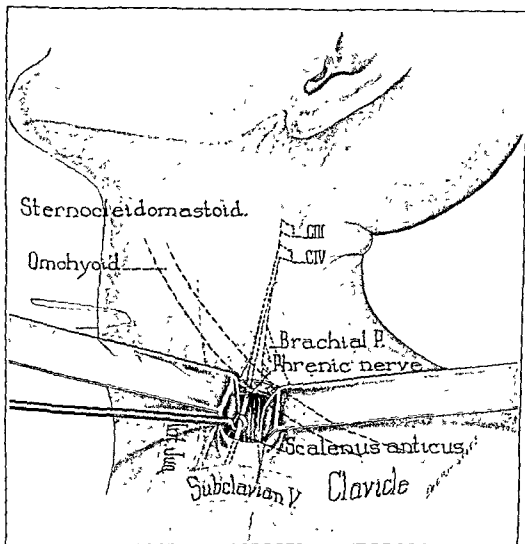


Plate V.—Authors' surgical approach to the phrenic nerve.

in such a case would probably lead to severe, if not fatal, bleeding; this type, fortunately, is not common. Friedrich encountered a phrenic nerve intimately bound to the internal jugular vein. The wall of the vein was torn in the process of exaïresis and a fatal air embolism took place.

In the complex types of phrenic, the *radical phrenic neurectomy* of Goetze alone appears practicable. Whether an exaïresis or radical resection is the operation of choice, will depend entirely upon the type of phrenic nerve met with at the time of operation.

*Technic of Operation.*—Based upon these anatomical studies, our surgical approach is through the subclavian triangle because of the accessibility to the associate fibers (Plate 5). We make an incision 2 to 3 cm. long, 2 cm. above and parallel with the clavicle, extending from the posterior border of the sternomastoid lateralwards, and enter the subclavian triangle below the omohyoid muscle. The platysma, superficial and deep fascia are divided; the external jugular is either ligated and cut or retracted. The pyramidal fat body, together with the small lymph glands usually met with, is retracted. Below, one will see the transverse scapular artery, and above, the superficial cervical artery; both of these cross the phrenic nerve transversely in front of it. The phrenic nerve is sought out on the anterior surface of the scalenus anticus, separated from the fascia and picked up with the tenaculum. After positive identification and further examination of the field for associate branches (the incision may be lengthened for this purpose), the nerve is injected with novocaine and resected. If no complex types are met with, an exaeresis is done by making gentle traction upon the nerve with the hemostat, or by winding the nerve upon a hemostat which is rotated upon an anatomical forceps. Should associate fibers be found, these are cut and an exaeresis of the main stem performed.

If the nerve is not adherent to other structures in the mediastinum, it slips from its sheath with ease. The patient is unaware of the procedure until the nerve disunites from the diaphragm, at which time a sudden "thud" is experienced in the region of the epigastrium. Evulsion is not accomplished so readily in many cases, especially if a mediastinal pleurisy has existed. In such instances, there is an increased resistance to traction after a few centimeters of fiber have been withdrawn, and the patient is likely to complain of pain, referred usually to the shoulder. If steady traction is maintained, the resistance gradually lessens and the pain disappears as a few more centimeters of nerve fiber slips from its sheath. When a mediastinal pleurisy has existed, resistance to traction may then again be encountered, frequently associated with pain throughout the corresponding side of the chest, or referred to the heart or epigastrium, and one will occasionally feel a distinct cardiac impulse transmitted through the nerve fiber. As resistance to traction lessens, and more nerve slips from its sheath, this pain, too, quickly disappears. If the nerve is not adherent to the mediastinum, a distinct diaphragmatic tug may be noted with each inspiration. In still another group of cases, the nerve is so densely adherent to the mediastinum that evulsion is impossible. The nerve either breaks (the distal end retracting into the thoracic cavity), or one is forced to cut it because of the fear of damaging important structures. Should this happen, the nerve is cut as low down as possible. If the section of nerve removed measures less than 10 cm., the operation is converted into a radical phrenic neurectomy by seeking out and removing a section of the nerve to the subclavius muscle, as well as all communicating fibers between the phrenic and the cervical nerves.

In closing the wound, the fibers of the deep cervical fascia and platysma are approximated with iodinated catgut, and the skin incision closed by means of an intracutaneous silkworm gut or horsehair suture.

## CHOICE OF OPERATION.

In the choice of operation, one must be guided by conditions met with at the time. It is our custom, in all cases, to attempt an exaïresis of the nerve according to the method of Felix, but if complex types of the nerve have to be dealt with, or the nerve is greatly resistant to evulsion, the fiber is cut as low down as possible and the operation converted into a radical phrenic neurectomy proposed by Goetze.

Under some circumstances one may wish to induce only a temporary hemidiaphragmatic paralysis and await the clinical effect before making the paralysis permanent. This is particularly true in some cases of extensive bilateral tuberculosis and in bilateral lower-lobe bronchiectasis.

In one case of extensive bilateral tuberculosis with uncontrollable hemoptysis, in which we could not be absolutely certain of the bleeding side, a pneumothorax was first attempted, and upon failure to introduce gas, we exposed the phrenic nerve and injected it with alcohol. The paralysis induced in this way lasted only a week, but the hemoptysis subsided immediately and the patient's decided clinical improvement persuaded us to believe that not only had the right side been selected but that a permanent paralysis was allowable.

A temporary paralysis can also be induced by crushing the phrenic nerve which is preferable to injections of alcohol when a more lasting paralysis is desired. We have seen several cases of bilateral lower-lobe bronchiectasis, where the only feasible method of effecting a collapse of the dilated bronchial tubes was by inducing a diaphragmatic paralysis. Since it is impossible to determine beforehand the clinical and anatomical effects of a hemidiaphragmatic paralysis in bilateral disease, we do not feel justified in inducing a permanent paralysis without having first determined the influence of a temporary one, particularly as to the rise of the diaphragm and its effect upon the quantity of expectoration raised daily. So in bilateral disease, it is our custom to crush the nerve on the worse-diseased side. After noting its influence, one can then crush the nerve on the other side or proceed immediately with an exaïresis. The paralysis on the side operated on first can later be made permanent. A second operation, however, is rendered much more difficult by the scar-tissue formation which may bury the phrenic nerve. In one of our cases of bilateral bronchiectasis of ten years' duration, in which the expectoration amounted to 80 c.c. daily, the right phrenic was first crushed, after which the expectoration dropped to 30 c.c. daily. Six weeks later the left phrenic was resected; the expectoration ceased completely. In the course of three months, the diaphragmatic function began to return on the right side. A permanent paralysis was then induced. This patient, a sixteen-year-old girl, has experienced a most remarkable clinical improvement. There is no expectoration and she is able to play tennis, swim, and indulge in all kinds of outdoor sports without any embarrassment of the respiration whatsoever.

Since 1924 we have operated upon more than 400 cases. The *phrenicus exaïresis* of Felix was attempted in all of them, but when the section of nerve fiber evulsed measured less than 10 cm., the operation was converted into a radical phrenic neurectomy of Goetze, by resecting a small section of the nerve

to the subclavius, as well as all communicating fibers. In some cases, accessory fibers (also the nerve to the subclavius) were not found. The operation consisted then of only a simple phrenic neurectomy.

In our first 150 operations there were 29 cases in which the nerve fiber removed measured less than 10 cm. and no accessory or communicating branches were severed. Of this number, subsequent observations were impossible in 18 cases because the patient either underwent a thoracoplasty, or dense diaphragmatic adhesions prevented a study of the diaphragmatic dome.

Notwithstanding, observations were carried on in 11 cases for from one to five and a half years. Of this number a return of function was noted in only 3 cases, all of which presented a hemidiaphragmatic paralysis immediately after operation, but showed a return of function in less than six months. In 8 of the 11 cases observed, the paralysis was still present one year later. The nerve fiber removed in all of these 11 cases measured less than 10 cm., and in 4 cases the nerve fiber removed measured less than 5 cm.

We note one case in which the nerve fiber removed was only 2.5 cm., yet the paralysis still existed three years later. In two other cases the nerve fiber removed measured 3.5 cm., and the paralysis persisted two years later.

We have never seen a return of function when the evulsed fiber measured 10 cm. or more. Our experience therefore tends to show that, if one evuls less than 10 cm. of nerve fiber and fails to sever accessory or communicating fibers, a return of diaphragmatic function can be expected in about 25 per cent. of the cases.

### COMPLICATIONS.

While exaeresis of the phrenic nerve is a minor operation, it is not without danger and should not be attempted by anyone not possessing a thorough knowledge of the topographical anatomy of the neck, and particularly a knowledge of the anomalies of the phrenic nerve. This is especially stressed by Sauerbruch<sup>2</sup> as a result of his observation of many cases operated outside his clinic, when the vagus, sympathetic and long thoracic nerves have been cut instead of the phrenic.

In our series of over 400 operations we have had no operative mortality or serious operative complications such as have been reported. Aside from a failure to find the phrenic nerve or to recognize its anomalies, the most serious complications to be contended with are damage to vascular structures, to important nerve structures, and to the thoracic duct. When the phrenic nerve exists in an anomalous form, much time may be spent in its search. This occurred in a few of our cases, and in one instance, as cited, we were unable to find the nerve.

Plenk and Ralph C. Matson,<sup>12</sup> in the course of their dissections, noted a unilateral absence of the phrenic in one case and a bilateral absence in another. Failure to find the phrenic nerve is also recorded in one of 150 cases operated in the Sauerbruch Munich Clinic.<sup>4</sup> It is possible that the phrenic nerve was absent in our case as well as in that of Sauerbruch.



In another referred case, the phrenic was reported to have been evulsed but our examination revealed a functionally intact diaphragm. A second operation revealed a phrenic occupying an anomalous position. Evulsion was followed by a hemidiaphragmatic paralysis. It is possible that a double phrenic existed in this case. Plenk and Matson observed a double phrenic in eight instances out of 112 dissections.

As attested by the experiences of some surgeons, *damage to blood-vessels* has resulted in serious complications. In our cases it has been rarely necessary to apply hemostats for the control of bleeding, but in 3 cases, following rupture of the nerve, there was considerable bleeding from the nerve sheath; upon application of hot packs, it rapidly subsided. In one case the bleeding occurred after about 7 cm. of fiber had been evulsed, and it became so active that, fearing an accessory branch was wrapped around some important vascular structure, the nerve fiber was cut. Bleeding from the pericardiophrenic artery, which under some circumstances might be damaged during the course of evulsion of the nerve fiber, has been reported.

The danger of *tearing into the subclavian vein* must always be considered since the accessory branch usually wraps around the subclavian vein to join the main stem of the phrenic nerve (Plates 1 b, c; 2 a, b, d; 3 b, d; 4 a, b). If this accessory branch is large or firmly attached to the main phrenic, there is danger of tearing into the vein during the course of evulsion. Plenk and Matson, in their dissections, as stated, discovered an accessory fiber coursing through the wall of the subclavian vein, and separated from the lumen only by the intima. Damage to vascular structures, in the course of evulsion of the phrenic, is common in dissections of the cadaver. Willy Felix ruptured the pericardiophrenic artery twice in 17 such dissections. Fortunately, in the living subject, the nerve fiber usually ruptures without damage to the more resistant connective-tissue wall of the blood-vessel. But unless the evulsion is accomplished with ease, the danger of tearing into an important vascular structure must be reckoned with. Sauerbruch<sup>2</sup> reports 3 severe hemorrhages in simple phrenic neurectomy; two of the patients died, and the third lived after ligation of the subclavian vein.

Sauerbruch<sup>12</sup> reported one operative death as a result of wounding the thyrocervical trunk, necessitating ligation of the subclavian artery. In another case, under similar circumstances, the subclavian artery was successfully ligated.

Friedrich<sup>14</sup> reported one death from air embolism as a result of tearing the wall of the internal jugular in attempting to separate the vein from the nerve to which it was bound by inflammatory adhesions.

The Sauerbruch Munich Clinic<sup>4</sup> reported 2 cases of air embolism occurring as a result of tearing into large venous channels. In one case the patient developed a paralysis of both arms. In the other there was a flaccid paralysis of one arm and a spastic paralysis of the other. In both instances the paralysis subsided in the course of a few days.

In one of our cases the wall of the internal jugular was torn, resulting in rather severe bleeding. Fortunately the rent was small and easily closed with a fine ligature.

*Hemoptysis*, occurring immediately after a *phrenicus exairesis*, has been reported, but we have not observed this complication in any of our cases.

Damage to the *sympathetic* or *vagus nerve* has been reported. Berg records one death under symptoms of a *vagus* and *sympatheticus* paralysis following exairesis of the phrenic nerve. Sauerbruch once observed a Horner symptom-complex following injury to the sympathetic. Brunner<sup>4</sup> saw a case in the Sauerbruch Munich Clinic in which, outside the clinic, the *vagus* had been erroneously cut instead of the phrenic. Sauerbruch<sup>2</sup> saw three more cases under similar circumstances.

We have seen one case of "*recurrens*" paralysis which was undoubtedly due to injury to the *recurrens* nerve in the course of a search for the phrenic. The paralysis subsided in the course of a few months.

The *thoracic duct* has been damaged frequently, although it has not occurred in any of our cases; such damage usually results in the formation of a chylous exudate beneath the skin wound. Drainage, or the application of hot packs or packing, generally suffices to stop the leak, but in some cases a chylous fistula may persist and death ensue from malnutrition.

Various psychic disturbances have been observed at the time of, or immediately following, the operation; these are of a temporary character and usually hastily disappear. Two of our cases developed a postoperative psychosis, and in one of these it persisted in a marked degree for several weeks. In another case, a highly neurotic and hysterical woman, who complained of much pain throughout the operation, claimed sudden utter inability to speak shortly after the dressings were applied. The patient remained mute for several hours, communicating by gesture, after which her speech suddenly returned.

Reflex disturbances of the heart and of the respiration have been observed in a few cases. In one case the patient developed a dyspnea, associated with a marked tachycardia; both persisted for several weeks. In another case the patient complained of vertigo during evulsion of the nerve, but after pausing a moment, the evulsion was completed without further disturbance.

Gastric symptoms, dyspnea and cardiac palpitation sometimes follow phrenic neurectomy, especially in cases wherein the left phrenic nerve has been evulsed, followed by a high diaphragm rise. These annoying complications have been carefully studied by Graham, Wilson, Singer and Balou.<sup>13</sup>

**Effect Upon the Diaphragm.**—After a complete interruption of nerve impulses to the hemidiaphragm has been effected, and if adhesions or thickening of the diaphragmatic pleura do not prevent, the diaphragm immediately assumes the expiratory position, and on quiet breathing, it is motionless under the fluoroscope. On deep inspiration it will rise slightly into the chest cavity as a result of the higher abdominal and lesser intrapleural pressure—a phenomenon known as "*paradoxical diaphragm movement*" described by Kienboeck. Bittdorf describes a test by which the paradoxical movement of the paralyzed diaphragm is still better educed: the patient is told to close the nares by pressing them between the fingers and then attempt to take a deep breath with the mouth closed. The paralyzed hemidiaphragm will rise into the thoracic cavity; on the non-operated side it descends.

Perhaps the most sensitive and easily applied test is the so-called "sniffing test" described by Hitzenberger,<sup>10</sup> elicited by directing the patient to "sniffle." The paralyzed hemidiaphragm rises into the chest, whereas on the other side it descends.

While the paralyzed hemidiaphragm, if not hindered, assumes the expiratory position immediately after operation, it continues to rise gradually throughout the ensuing months as muscle degeneration and atrophy progress. This is still further accentuated by the shrinkage of scar-tissue as healing in the lung progresses. The maximum rise may not be attained for from six months to a year or more. In our 400 operated cases, the highest rise noted was 13 cm on the left side two years after operation. In this case the initial rise immediately after operation was 3 cm. At the end of one year, the diaphragm had risen 9.5 cm. The rise measured 13 cm. at the end of two years. On the right side, the highest rise noted was 8.5 cm. one year postoperatively.

It must also be pointed out that, even though the diaphragm is apparently fixed by adhesions and exhibits no motion under the fluoroscope, and even though there is no rise immediately following the operation, as the diaphragmatic musculature atrophies and scar-tissue in the healing lung shrinks, a rise gradually takes place and may reach its maximum in a year or more. In one of our cases there was no rise immediately after operation, but at the end of nine months the rise amounted to 8 cm.

**Reduction in Lung Volume.**—It is generally admitted by all authorities that the collapse provided by satisfactory pneumothorax may be total. The collapse provided by a thoracoplasty, even under the most favorable circumstances, cannot possibly be total, but may very closely approach it. The collapse provided by a hemidiaphragmatic paralysis under the most favorable circumstances can amount to scarcely more than a reduction of one-sixth to one-third of the lung volume, according to Brunner's<sup>4</sup> experiments.

**Effect Upon the Lung.**—The results of an induced hemidiaphragmatic paralysis are less dependent upon the site of the lesion than upon its type. This is explained by the fact that in certain types of tuberculosis, particularly the *proliferative varieties*, the capacity for collapse of the diseased lung tissue is greater than that of healthy lung tissue. Therefore, even though the lesion is in the upper lobe, the rising diaphragm, by reducing the volume of the hemithorax, permits the collapse capacity of the diseased lung tissue to exert itself, even without any collapse of healthy lung tissue.

Years of observation in pneumothorax therapy support our belief that in the productive types of tuberculosis the collapse capacity of the diseased lung tissue is greater than that of healthy lung tissue; we have seen that the diseased lung tissue almost invariably collapses before healthy lung tissue, in the absence of adhesions. As a matter of fact, in some cases observed over a period of many years, the healthy lung tissue has always been in contact with the chest wall, the diseased lung tissue alone being collapsed.

The results of an induced hemidiaphragmatic paralysis are more dependent upon the rise of the diaphragm and the degree of collapse of diseased lung tissue affected thereby than upon merely placing the diaphragm at rest. Our belief that

the beneficial influence of hemidiaphragmatic paralysis is due to the degree of collapse of diseased lung tissue affected by the rising diaphragm, rather than the rest provided, is based upon the observation that the best results have always been associated with a marked rise of the diaphragm, and the poorest results have been in those cases in which little or no rise of the diaphragm took place (Table I). In cases in which the diaphragm does not rise, a roentgenological

TABLE I

	Average Rise of Diaphragm
11 cases, 35 per cent, much improved	3.5 Cm.
9 cases, 28 per cent, improved	2.8 Cm.
10 cases, 36 per cent, unimproved	1.8 Cm.
2 cases, unimproved	7.0 Cm.

In 13 cases (40 per cent), the sputum became negative for tubercle bacilli.

18 cases received a thoracoplasty.

In 11 cases (35 per cent.) thoracoplasty became unnecessary.

study will show that if not absolutely motionless, it moves but 1 or 2 cm. on full inspiration, and is essentially at rest on ordinary breathing.

The rise of the diaphragm and the collapse of diseased lung tissue are dependent upon the character and extent of adhesions, as well as the type of tuberculous lesion. The more the pulmonary lesion tends to the proliferative type, the greater the collapse capacity of the diseased lung will be. Contrariwise, the more the lesion tends to the exudative type, the less the collapse capacity of the diseased lung will be; the most favorable results are noted in those lesions which are predominantly proliferative. Even though the collapse capacity of the diseased lung tissue is great, a collapse may be prevented by adhesions (particularly interlobar or adhesions between the parietal and visceral layers of the pleura), or thickening of the diaphragmatic pleura which prevent a rise of the paralyzed diaphragm. In upper-lobe lesions, if the lung is densely adherent to the chest wall, or interlobar adhesions exist, there may be no collapse of diseased lung tissue, even though one obtains an excellent rise of the diaphragm.

#### CLINICAL EFFECTS.

The beneficial influence of a satisfactory hemidiaphragmatic paralysis is manifested clinically, first, in the marked reduction of the amount of expectoration. During the first few days after operation there may be a decided increase in sputum, due to the expulsion of retained secretions from the diseased lung tissue, but following this the quantity of sputum diminishes rapidly. This initial increase in quantity is particularly apparent in the case of lower-lobe lesions. We have in mind a case of bilateral bronchiectasis in which the average daily expectoration amounted to 200 c.c. An exaeresis of the phrenic nerve was done on the worse side, following which the expectoration dropped in the course of three months to 50 c.c. daily. Similar exaeresis was then done on the contralateral side—after this, the expectoration increased during the first twenty-four hours after operation to 150 c.c.; on the second day it amounted to 110 c.c., and

on the third day 70 c.c. Since that time, the expectoration has diminished constantly until at present (six months after operation), the patient is without expectoration.

The reduction in the sputum quantity is often astonishing. In a case of chronic upper-lobe abscess, in which the average daily expectoration amounted to 750 c.c. during a period of several months' observation, the sputum decreased immediately after operation, and at the end of three months there was no expectoration.

In another case of chronic upper-lobe abscess in a man 50 years of age, during a month's preoperative observation, the daily average maximum temperature registered 102° F. The expectoration amounted to 200 c.c. of foul, fetid secretion. Three weeks after operation the temperature was normal and the expectoration had ceased entirely.

In pulmonary tuberculosis, one can scarcely hope for such striking results because of the nature of the disease. Nevertheless, our records are replete with cases in which an average daily sputum of 60 c.c. to 80 c.c. has entirely disappeared in the course of a few months after operation. Not only is there a marked reduction in the quantity of sputum, but there is also a disappearance of tubercle bacilli. It is not at all uncommon to find tubercle bacilli absent from the sputum, even after a few weeks or months following operation, whereas they had been previously present in enormous numbers.

Contrary to the early general belief that a paralyzed diaphragm would impair the ability to cough effectually, thus endangering the patient to serious complications from the retention of secretions or the aspiration of sputum into healthy lung tissue through his inability to "raise," the reverse is true. The ease with which expectoration is raised is a matter referred to voluntarily by the patient.

As an example, we might again allude to the case of bilateral bronchiectasis just mentioned. Following the second operation the patient, when interrogated regarding his expectoration, remarked smilingly that he raised his expectoration now without any effort, whereas previously he had experienced violent coughing paroxysms.

The ability to "raise easier" following operation is not difficult to understand, since the expulsion of secretions through coughing is brought about through the action of the abdominal muscles, and it is therefore far more easily accomplished after the resistance of the natural diaphragmatic tonus has been abolished.

Aside from the reduction of sputum and the facility of expectoration, the most impressive clinical effect, following a satisfactory hemidiaphragmatic paralysis, is the rapid disappearance of fever, which is a most gratifying and convincing proof of the value of this simple procedure. The reduction of fever may begin twenty-four hours after operation and continue, in favorable cases, day after day, until the temperature completely reverts to normalcy. The reduction of fever is attributed to the blockage of lymph channels and consequent stagnation of the lymph stream as a result of the collapse and rest provided to the diseased lung tissue, thus inhibiting the absorption of the tuberculotoxic products.

Coincident with the reduction of fever and the diminution of expectoration, a corresponding improvement in the general condition of the patient takes place. The appetite improves, the weight increases, fatigue subsides, the secondary anemia disappears, and the patient looks and feels much better.

### RESULTS.

Operative procedures upon the phrenic nerve are indicated under a wide diversity of conditions in the treatment of pulmonary tuberculosis, as well as in nontuberculous pulmonary suppuration. In the treatment of pulmonary tuberculosis the operation is indicated not only as an adjunct to other surgical treatment but as an independent procedure. Unfortunately, most of the statistics published heretofore dealing with the results of phrenic-nerve surgery have been of little value because the authors have failed to classify their cases properly, or they have neglected to supply other information which would enable the reader to arrive at an independent conclusion.

A discussion of all types of disease and classes of cases in which we have induced a hemidiaphragmatic paralysis is not within the scope of this chapter. We shall therefore confine ourselves to a review of 66 cases of the productive type of tuberculosis, in which a pneumothorax was attempted and failed because of pleuritic adhesions. All of these patients were suffering from far-advanced tuberculosis (N. T. A. III). Most of them were experiencing an acute exacerbation of their disease, so were actively febrile and suffering from marked loss of weight and strength. The sputum was positive for tubercle bacilli in 63 of the 66 cases, 3 having denied expectoration, although the radiograph showed extensive lesions with excavation. The average daily amount of expectoration was 30 c.c. In 2 cases it amounted to more than 100 c.c. With one or two exceptions, all cases had demonstrable excavation of lung tissue on the operated side, and in many cases a large cavity, measuring from 4 to 5 cm. by 6 to 8 cm., was present. In 2 cases the cavity measured 6.5 cm. by 8.5 cm. Even though the entire lung was involved, the disease exhibited the characteristics of only an upper-lobe lesion in all cases. No distinctly lower-lobe lesions are included in this series, as they are classed separately and will be dealt with in a future contribution. All cases included in this series were operated on since 1924 and no case has been included which has undergone operation more recently than January, 1929. To accumulate accurate data, we have endeavored to keep in close contact with all living cases, and especially to obtain from them frequent roentgenological examinations as well as measurements of sputum.

Preceding every operation is a fluoroscopic study of the diaphragm, in order to determine its mobility, supplemented by radiographs taken at the height of inspiration and at extreme expiration, to determine its excursion, and upon which is based a measurement of the distance from some anatomical point (usually the transverse process of the first dorsal vertebra) to the dome of the diaphragm and a measurement of the dimensions of excavated areas. The patient is fluoroscoped and filmed again, usually immediately or within forty-eight hours after operation. Under the fluoroscope the patient is subjected to various tests for hemidiaphragmatic paralysis (the Hitzenger test is the most

sensitive and easily applied). The radiograph is compared with that made immediately before operation and the rise of the diaphragm is noted, as well as changes in the dimension of excavated areas.

Reexaminations, supplemented by the use of the fluoroscope and the radiograph, are made at intervals of at least one month during the first three to six months, and at intervals not exceeding three months during the subsequent period of observation, which, in each case, is carried on as long as possible. In some cases, because of extraneous circumstances, we have had to content ourselves with less frequent examinations, especially after the first year. Post-operative observations have been impracticable in still other cases, but those are naturally not included in our study.

Daily measurement of expectoration quantity is carried out for two weeks after operation—then at weekly intervals for three months, after which the measurement of an average twenty-four-hour specimen once a month is sufficient. The microscopic examination of the sputum is usually made once a

TABLE II

	Average Rise of Diaphragm
18 cases, 52 per cent., much improved	5.4 Cm.
12 cases, 38 per cent., improved.	3.0 Cm.
2 cases, 5 per cent., unimproved	3.5 Cm.
2 cases, 5 per cent., worse	6.7 Cm.

5 cases, 44 per cent. (much improved): Sputum became negative for tubercle bacilli.  
 15 cases, (much improved): Had large cavity in upper lobe which disappeared.

month. The estimation of the germ content, according to some scale, is of value when done by a well-trained technician. If the sputum is negative to the tubercle bacillus after a search of 200 fields covering a period of approximately fifteen minutes, the twenty-four-hour specimen is concentrated and the residue examined.

For convenience, we have divided this group of 66 cases into two classes as follows:

First, those cases in which the disease was predominantly unilateral and a thoracoplasty was contraindicated (34 cases).

Second, those cases in which the disease was essentially unilateral and a thoracoplasty was indicated (32 cases).

In the predominantly unilateral types of tuberculosis, a thoracoplasty was contraindicated because of the presence of active or progressive disease in the contralateral lung. In most instances this disease was associated with demonstrable excavation. Aside from that, many cases were also bad surgical risks because of their age or serious complications such as tuberculous enteritis, malnutrition, diabetes, atrophy of the heart associated with marked dyspnea on the slightest exertion, due to long-standing tuberculous infection, etc. The results of operation in this group of 34 cases were as seen in Table II.

In the 18 cases, 52 per cent., "much improved," a thoracoplasty became unnecessary, which is a very gratifying result when the type of disease is taken into consideration. All cases rated as "much improved" are capable of making a clinical recovery, and all, at the present time, are able to pursue occupational activities. None of these patients have any subjective symptoms, such as fever, fatigue, etc.; their lost weight has been regained, and the sputum, if present, has continued to be negative for tubercle bacilli after concentration methods of examination. The relationship of a good diaphragmatic rise to a satisfactory end-result is apparent in the above group.

Twelve cases, 38 per cent., are rated as "improved." In all of these, the sputum, although decreased in quantity, is still positive for the tubercle bacillus and even though most of these patients are afebrile and up and about (and many have resumed partial occupational activities), they are for the most part not likely to make a clinical recovery, unless other surgical measures can be or are resorted to. Most of these cases must be considered as going through a "quiescent period" of their disease and are likely to experience an exacerbation sooner or later. Nevertheless, incidental to the disappearance of fever, restoration of weight, etc., there has been an improvement in the general condition of all of these cases.

A serious hemoptysis, which was threatening the life of the individuals in two cases, ceased immediately after operation. In most of them there was a marked diminution of expectoration as well as of bacilli in the sputum. Three cases so improved that a thoracoplasty was possible, and several others are now in satisfactory condition for further operative procedure.

Obviously, one must be extremely cautious in attributing improvement or the relief of certain symptoms to the operation, as too often these changes take place as a result of other factors. This was particularly noticeable in one case in which an extensive unilateral lesion with demonstrable excavation existed. The sputum amounted to 100 c.c. daily; the patient was actively febrile and had experienced great loss of weight. Shortly after operation she moved to a distant point and reexamination was not possible. However, two years later, through correspondence, we learned that her condition was excellent; that she was afebrile, had gained 40 pounds in weight, was doing her housework, and that her sputum had diminished from 100 to 10 c.c. daily. Through her local physician we succeeded in obtaining a radiograph which was compared with the original, as a result of which we found that there had been no rise of the diaphragm and that, in spite of this marvelous improvement reported by the patient, the pulmonary pathological process had actually steadily progressed and the excavated area upon the operated side had also enlarged considerably.

Shortly after operation, in two cases, the disease, which was of an active, progressive, productive type, became rapidly progressive and of an exudate type. Rapid excavation of lung tissue, leading to bronchogenic extensions into the contralateral lung, took place in both instances; their diaphragmatic rise was 8.5 and 5 cm. respectively. Whether or not the rise of the diaphragm was responsible for this change in the type of pathological process, we cannot say. A somewhat similar experience is reported by Dumarest and Berard,<sup>17</sup> who



state that in 8 instances out of 107 cases, a very progressive course was assumed by the disease immediately after operation. The exacerbation in their cases was mostly of a mild type, but extension to the contralateral lung occurred immediately after operation in 2 cases, terminating fatally.

The relationship of the diaphragmatic rise to the behavior of the sputum is evident in a comparative study of 15 of the 18 cases described as "much improved."

In the second group in which the disease was essentially unilateral, the operation was done as a routine procedure preliminary to a thoracoplasty, a custom which we have long practised.

In the productive types of tuberculosis where an artificial pneumothorax is impossible and a thoracoplasty is indicated, an exaeresis of the phrenic nerve should be done as a preliminary procedure at least one month before the major operation is attempted, for the following reasons:

1. The improvement following an induced hemidiaphragmatic paralysis may lead to recovery, thus sparing the patient the necessity for a major surgical operation.
2. In favorable cases the patient is rendered a far better surgical risk because of the marked improvement which follows a satisfactory hemidiaphragmatic paralysis.
3. Not only is the quantity of sputum reduced but the cough is made easier, thus lessening the danger of aspiration infection, should a thoracoplasty be resorted to. (As a result of this beneficial influence, it is our custom to do an upper-phase thoracoplasty first in upper-lobe lesions, as we have no fear of retention or aspiration of sputum, the danger of which has probably withheld many surgeons from doing the upper phase first.)
4. To effect as much collapse as possible through the rising diaphragm, thereby reducing the number and amount of ribs later to be removed.
5. To permit the heart to partially accommodate itself to the increased functional activity later to be imposed upon it by a thoracoplasty.
6. As a test of the integrity of the contralateral lung.

One of the most difficult procedures in the surgical treatment of pulmonary tuberculosis is the correct evaluation of the status of the contralateral lung, since there are no means of knowing beforehand the demeanor of a suspicious lesion after having been subjected to the stress of a thoracoplasty.

In cases with suspicious changes in the better lung (particularly apical adhesions), a phrenicotomy, according to Sauerbruch,<sup>2, 6, 18</sup> is of value chiefly as a "test" operation before a thoracoplasty. If the operation is followed by an increase of the physical or roentgenological findings or fever, or the patient's general condition becomes worse, an extrapleural thoracoplasty is absolutely contraindicated. On the other hand, if there is no reaction, one may safely proceed with the major operation.

Lange<sup>4</sup> studied the diagnostic value of a phrenic neurectomy as a "test" operation in 23 cases in the Sauerbruch Munich Clinic, and found that in 12 "doubtful" cases a thoracoplasty had been decided upon after the "test" operation had failed to provoke any essential changes in the healthier lung. Subsequent observations in these cases showed that the test operation failed in but one case.

In our opinion a phrenic neurectomy serves as a "test" operation only in those cases in which a satisfactory rise of the diaphragm is followed by an exacerbation of disease in the better lung, and even then the test is not infallible.

Furthermore, an absence of changes in the better lung by no means indicates its behavior after a thoracoplasty. This belief is founded upon observations made in our first 65 thoracoplasties, in which a phrenic neurectomy preceded the major operation at an interval varying from one month to one year. Of these 65 thoracoplasties, 8 developed changes in the contralateral lung in the immediate postoperative period. Of this number, only 5 cases are of interest, and of these only 4 were of a "doubtful character."

CASE 1 S.D. Productive type of tuberculosis with excavation of right lung. Upon roentgenological examination, the left lung was found negative, but the physical examination showed an active infiltration of the upper lobe. One year after the "test" operation, with a diaphragmatic rise of 3.5 cm., the contralateral lung lesion was quiescent from a physical diagnostic standpoint and still negative roentgenologically, but following a thoracoplasty it became rapidly progressive.

CASE 2 R.H. Productive type of tuberculosis with excavation of left lung; apparently quiescent productive type of infiltration upper lobe right lung. Five months after the "test" operation, the contralateral lung lesion had been uninfluenced by a 4.5 cm. rise of the diaphragm. An upper-phase thoracoplasty, from which the patient made an uneventful post-operative recovery, was followed by an exacerbation of disease in the contralateral lung.

CASE 3 V.M. Productive type of tuberculosis with enormous excavation of left lung, apparently quiescent productive type of infiltration of upper lobe of right lung. Following the "test" operation, with a diaphragmatic rise of 3.5 cm., the contralateral lung lesion became active and later (after a few months) again quiescent. Following a complete thoracoplasty, the contralateral lung behaved in a similar manner.

CASE 4 A.H. Productive type of tuberculosis with enormous excavation of right lung, contralateral lung essentially negative. Sputum 80 c.c. daily. The immediate diaphragmatic rise following the "test" operation measured 3 cm. One month later the patient developed a serofibrinous pleurisy on the contralateral side. Following absorption of the exudate, roentgenological and physical diagnostic changes persisted for seven months. At the end of one year, the diaphragm had risen 6 cm. There was, however, no collapse of the excavated area. The sputum measured 90 c.c. daily. Following a thoracoplasty performed at this time, the contralateral lung lesion exhibited no change.

CASE 5 T.J. Productive type of tuberculosis with large excavation of left lung; bronchogenic infection of middle lobe of right lung. The diaphragm rose 7 cm. in one year, following the "test" operation, and the contralateral lung lesion disappeared completely from a roentgenological and physical diagnostic standpoint. Following an upper-phase thoracoplasty, the patient developed an aspiration infection into the lower lobe of the contralateral lung.

A study of our material indicates that the result of a phrenic neurectomy as a "test" operation must not be given excessive credence. In the first two cases of the above 5, we found that a contralateral lung lesion withstood the "test" operation but exhibited activity following a thoracoplasty. In the third case a contralateral lung lesion behaved similarly after both the "test" operation and the thoracoplasty. Disease was evinced in the fourth case by an essentially negative contralateral lung, following the "test" operation, but it passed through a complete thoracoplasty undamaged, although the excavated area was essentially the same before each procedure. In the fifth case a contralateral lung lesion disappeared after the "test" operation, but the thoracoplasty was followed by a lesion of similar type in a different location.

The remaining 3 cases are of no interest because the disease in the contralateral lung was due to an aspiration infection following the thoracoplasty.

All thoracoplasty cases are of course urged to rid themselves of secretions immediately before operation, but in the immediate postoperative period the ability to raise varies with the individual. In some cases secretions are aspirated into the healthier lung and expectorated without harmful influence, but in others, an aspiration infection follows. The nature of this complication is such that it is obviously impossible for a "test" operation of this character to supply information of value concerning the effect of the sudden closure of large excavated areas or the influence of the aspiration of sputum into the healthier lung.

The results of operation in this group of 32 cases were as seen in Table I.

In the classification of these end-results we have adhered to the rule applied in the first group. Therefore, all cases recorded as "much improved" are capable of a clinical recovery. The expectoration, if present, is negative for tubercle bacilli, and all patients are carrying on full occupational activities.

Of greatest significance is the fact that 11 cases, 35 per cent., of these patients, were so improved that a thoracoplasty became unnecessary. These results alone justify the operation as a routine preliminary before every thoracoplasty.

Nine cases, 28 per cent., were improved, inasmuch as there was a marked reduction of the daily expectoration, relief from fever and gain in weight, but a clinical recovery was, or is, extremely improbable without further surgical intervention.

Of the 9 cases improved, four received a thoracoplasty, four refused thoracoplasty, and in one case the improvement is so steady that a thoracoplasty is unwarranted.

An unusually large number of cases (12 to 37 per cent.) are recorded as unimproved for the reason that we have evaluated end-results only after the lapse of a reasonable time, at least six months to one year, because changes occurring in the immediate postoperative period (up to three months), even though of a favorable character, are often only of a temporary nature and permit no reliable conclusion as to the probable ultimate outcome.

All of the 12 unimproved cases received a thoracoplasty at intervals varying from one month to one year. The average diaphragmatic rise for 10 of the 12 cases was only 1.8 cm. In only 2 cases was there any essential change in the amount of expectoration following the induced hemidiaphragmatic paralysis. In one case the sputum dropped from 25 to 4 c.c. daily in the course of a year, but it was still positive for tubercle bacilli, and a comparison of radiographs showed a marked increase in the size of the excavated area. In the other case, with a very extensive unilateral lesion, the sputum became negative, but there was no rise of the diaphragm and no changes in the pulmonary pathological process from a radiographic standpoint. The absence of tubercle bacilli from the sputum was therefore considered to be of a temporary nature.

In 2 cases recorded as unimproved, there was an excellent rise of the diaphragm (8 cm. and 6 cm. respectively), but the quantity of sputum in both cases was unaffected and remained at 50 c.c. daily. In both instances there was a large cavity in the upper portion of the upper lobe, which was held open by dense thickening of the overlying pleura, as well as interlobar adhesions.

## SUMMARY AND CONCLUSIONS.

1. The operative technic, anomalies of the phrenic nerve, dangers of operation, operative complications, and effect upon the lung and diaphragm are discussed.

2. An *exairexis* of the phrenic nerve is the operation of choice. However, if less than 10 cm. of nerve fiber have been evulsed, a return of diaphragmatic function can be expected in 25 to 30 per cent. of all cases, unless all communicating or accessory fibers have been resected.

3. The beneficial influence of an induced hemidiaphragmatic paralysis is ascribed to the collapse of diseased lung tissue affected by the rising diaphragm rather than to the rest provided. This conclusion is based upon the observation that the most satisfactory results were seen in those cases presenting a high diaphragmatic rise, whereas the worst results were obtained in those exhibiting little or no rise of the diaphragm.

4. The most important clinical effects are a reduction of the sputum quantity, facility of expectoration, reduction of fever, and improvement of the patient's general condition, coincident with the disappearance of the above symptoms.

5. A pneumothorax had been attempted in all cases, and had failed because of the presence of pleuritic adhesions. In 34 cases a thoracoplasty was contraindicated because of the state of the contralateral lung, etc. In 52 per cent. of these cases the patient so improved that a thoracoplasty became unnecessary. In 32 cases a thoracoplasty was indicated, and in 28 per cent. of these, the patients so improved that a thoracoplasty was unnecessary.

6. The sputum became negative for tubercle bacilli in 42 per cent. of the cases.

7. The induction of a hemidiaphragmatic paralysis, either by *exairexis* or radical resection of the phrenic nerve, is strongly recommended in all patients for whom a pneumothorax is indicated and adhesions prevent the introduction of gas.

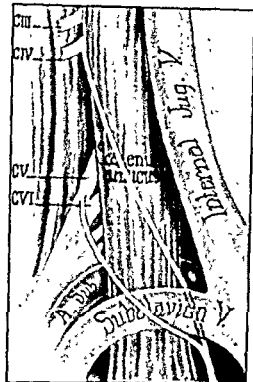
8. The operation is indicated (1) as an independent procedure in those cases in which a thoracoplasty is impossible, (2) as a preliminary to every thoracoplasty.

9. Too much dependence cannot be placed upon the result of a phrenic neurectomy as a "test" operation.

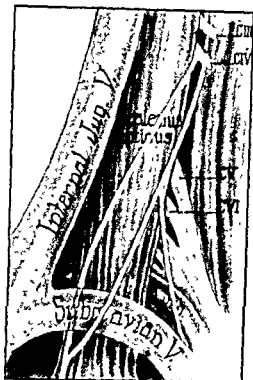
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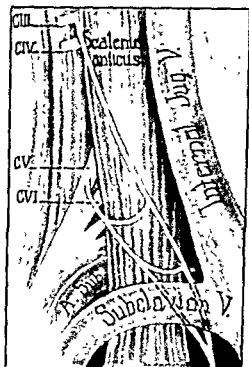
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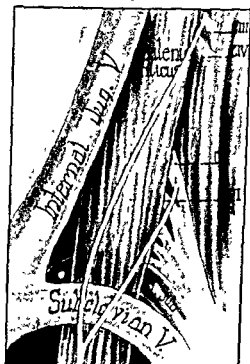
a



b



c



d

Plate IV—(a) Phrenic from *civ* and associate phrenic from *cv* passing in front of subclavian vein. A dangerous type for exauresis. (b) Phrenic arising from *civ* by two trunks of equal size. One passes over the anterior surface of the scalenus anticus and behind the subclavian vein; the other arises lateralward from *civ* and passes over the lower portion of the scalenus anticus and in front of the subclavian vein. A dangerous type for exauresis. (c) Phrenic arising from *ciii* with branches from *cv*. (d) Phrenic from *ciii* and *cv* passing in front of subclavian vein.

in the third intercostal space midaxillary line and its jaws clamped down on the remaining portion of the adhesion which was then thoroughly electrocoagulated. Cutting was then carried out without any loss of blood, no further electrocoagulation being necessary. Complete collapse of the lung followed.

The quantity of the patient's sputum promptly diminished, so that after two weeks the daily quantity ranged from 0 to 3 c.c. During the course of these operations, a progressive improvement also took place in the opposite lung and larynx.

The danger of thrombosis of the vessel from heat of the galvanocautery and inflammatory reactions, as well as sloughing of tissue, has been pointed out in connection with cutting adhesions situated close to large blood-vessels. In

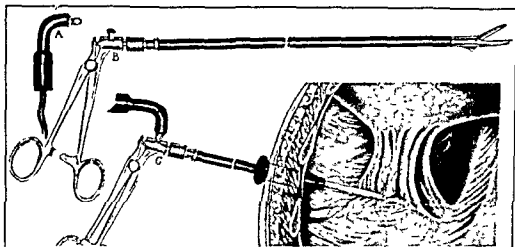


Fig. 69.—Author's intrathoracic hemostat.

A. Tip of cable connecting instrument with high-frequency unit.

B. The hemostat.

C. Diagram showing the instrument applied to a portion of a highly vascular spool adhesion for electrocoagulation preliminary to cutting.

numerous cases, we have cut adhesions so situated which would not have been attempted with the galvanocautery.

*Resumé.*—In our series of 249 cases, serosanguineous exudate occurred twenty-seven times. This includes all cases wherein the postoperative effusion revealed fluid containing blood. In some cases, the amount of blood-tinged exudate measured as little as 100 c.c., while in others, several hundred cubic centimeters were found. In 14 instances, hemorrhagic exudate followed the use of the galvanocautery. Of the others, 11 followed the use of the old type high-frequency unit, while only one occurred when the Bovie unit was employed (this case has already been referred to). In only one instance did any bleeding occur in cutting a cord adhesion. In 18 instances of bleeding, the operation had to deal with fold, diffuse and spindle types of adhesions. Bleeding at the time of operation was responsible for hemorrhagic exudate in 16 cases; all were fold, diffuse or spindle types of adhesions, where a complete operation was impossible

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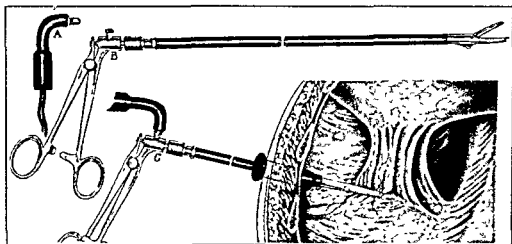


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because of the nature of the adhesions. In 7 cases, slight bleeding took place during the section of large band adhesions. In 10 cases, no bleeding occurred at the site of operation, but did take place at the site where the thoracoscope or operating instruments had been introduced. Consequently, in the description of the technic, attention is called to the importance of a thorough infiltration of the endothoracic fascia with the novocaine-suprarenin solution, and the necessity of directing the approach of the trocar and cannula for the operating instruments by thoracoscopic observation. One can visualize the point where the trocar depresses the pleura before it is punctured. In case it should be too close to the rib, its direction can be changed. The operator must, of course, always be mindful of the distribution of blood-vessels in the chest wall, and select sites for puncture where damage is unlikely to the intercostals, the internal mammary as well as the long thoracic vessels.

Attention has already been directed to the vascularity of the different types of adhesions in the classification of them. One can be assured, from our histopathological studies, that dangerous bleeding will not be encountered in cord and band adhesions. Bleeding is most likely to occur in severing spool adhesions at the chest wall; also spindle, fold, and attempts to improve the lung collapse by severing parts of diffuse adhesions, are likely sources of bleeding. The cutting of the latter type should be attempted only after one has had experience with the less dangerous kinds of adhesions.

Bleeding, in our cases, has almost invariably been from the chest wall stump; it had to do with cases wherein it was necessary to cut close to the chest wall to avoid lung tissue, leaving no chest wall stump. The contraction of the lung stump, which always follows cutting, unless it is densely organized, undoubtedly prevents bleeding. It should be borne in mind that while old, fibrinous adhesions are likely to have obliterated blood-vessels, one occasionally meets with large blood-vessels in their interior, as in Cases 2 and 3, where profuse hemorrhage occurred. Again, it should be repeated that the closer the cutting is to the chest wall, the greater is the danger of bleeding; but this statement must not encourage one to cut further away, because of the danger of cutting into prolongations of cavities or lung parenchyma.

If the adhesion is to be cut close to large blood-vessels, the operation must be undertaken with serious forethought and thorough knowledge of the anatomy of this site. Cutting adhesions attached to the pleural cupola, when a thickened pleura obscures the subclavian vessels, also severing adhesions in the costo-vertebral gutter and near the internal mammary vessels, should be approached with great caution.

Bleeding, while using the electrosurgical method, can be almost entirely prevented, but should it occur after having electrocoagulated the tissue, the bleeding point must be "touched up" with the coagulating current; if fairly profuse, one can arrest it most successfully by holding the electrode tip a few millimeters away and spraying the bleeding area with sparks. If still uncontrolled, the pointed operating tip should be pushed into the tissue immediately adjacent to the bleeding vessel and a deep coagulation made (Case 2). If this

procedure fails to check the hemorrhage, an urethral forceps, which, in the absence of the author's hemostat, should be part of the armamentarium, must be clamped upon the vessel and the coagulating current applied to it. However, should even this be unsuccessful, one must consider transfusion and open operation for direct ligation of the bleeding vessel.



Fig. 70.—Pneumothorax of five months' duration. Sputum 10 to 25 c.c. daily—constantly positive. (1) Band adhesion preventing closure of cavity (2). Curtain adhesion (3).

#### RESULT OF TREATMENT.

In our series of 249 cases, a single operation was done in 211 cases, in 22 instances two operations were performed; 10 cases had three operations; 4 cases had four operations, and 2 cases had five operations each.

In estimating the value of the operation, it must be remembered that the purpose of the operation is to convert a useless or unsatisfactory pneumothorax

into an efficient one. Accordingly, the results of operation have fundamentally to do with the number of unsatisfactory pneumothorax cases which were converted into satisfactory ones, but we are more concerned in the ultimate result of the operation or end-result of the pneumothorax thus established. Every case classified as "clinically and technically successful" from the standpoint of the operation, signifies that complete severance of all adhesions, followed by

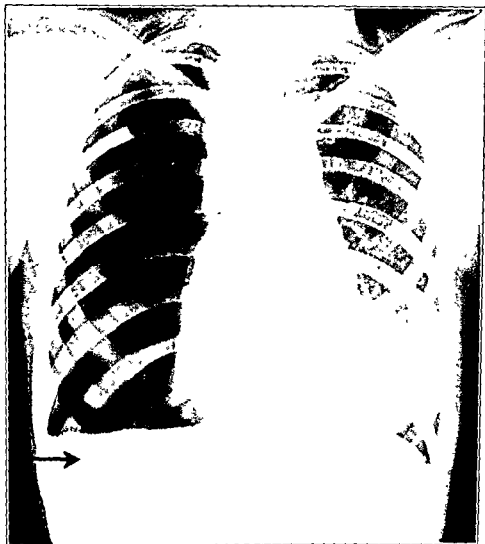


Fig. 71.—Same case as Fig. 70. Six days after operation. Sputum diminished. A positive sputum was never found after operation. Three years later patient clinically well.

a satisfactory pneumothorax with prompt, sometimes immediate, disappearance of severe cough and expectoration was obtained (Figs. 70 and 71).

Of the 249 cases, one hundred and fifty-two, 61 per cent. were technically and clinically successful. Of these, 32 cases had to deal only with string and cord adhesions. In 85 cases, band adhesions alone were present; in 22 cases, the other types of adhesions, excepting arachnoid and diffuse adhesions, were

present. The common statement that only small adhesions "the size of one's finger" (quotation from a standard treatise on the Surgery of Pulmonary Tuberculosis) are suitable for operation must be challenged. The author has repeatedly severed adhesions 8 to 10 cm. wide and 2 to 4 cm. thick (Figs. 72 and 73).

The technically unsuccessful, but clinically successful group comprises 19 cases presenting all the above types of adhesions, as well as others described



Fig. 72.—Large complex band adhesion preventing sufficient collapse of the lung in a pneumothorax of six months' duration. Sputum 20 to 30 c.c. Tubercle bacilli positive

under the classification of adhesions. This group comprises cases in which some adhesions, because of their character, were left uncut, yet sufficient collapse of the lung was obtained to bring about a satisfactory clinical result by electrocoagulation (Figs. 74 and 75). The adhesions referred to in the above group as not suitable for operation were of the diffuse type. The possibility of success in such cases is usually so slender that operation should be under-

taken only under extraordinary circumstances, and then only by experienced operators.

It has been pointed out that clinical success is not always dependent upon cutting all adhesions. It should be determined which are of technical importance, and these severed. Technically important ones, if of an unfavorable type for

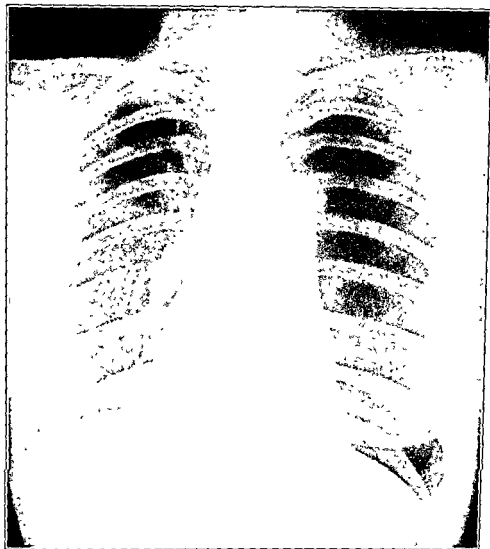


Fig. 73.—Same case as Fig. 72. One week after operation. Sputum 5-10 c.c. T.B. positive. No reaction to operation. One month later no cough or expectoration.

operation, should be left undisturbed. Of the 249 cases forming a basis of this study, 171 (70 per cent.) obtained a clinically successful result.

The technically successful, but clinically unsuccessful cases were two, one of which, previously quoted, died apparently from a spontaneous pneumothorax seven days after a third operation, and the other of sudden profuse hemorrhage from the successfully collapsed lung which, due to her position, with the pneumothorax side up, filled the dependent sound lung. Seventy-six cases constitute

the technically and clinically unsuccessful group; 46 of these presented only diffuse adhesions and 34 had diffuse adhesions in combination with others of string, cord or band type. These latter were severed, but the remaining diffuse adhesions prevented a satisfactory collapse of the lung. Some of these cases were later subjected to phrenic neurectomy and thoracoplasty.

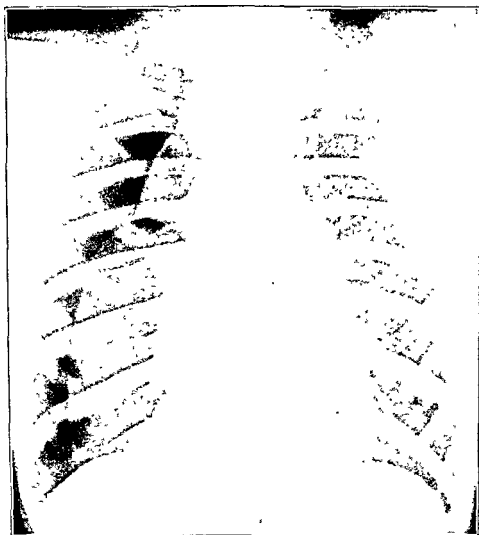


Fig 74—Uncollapsed cavity in spite of a pneumothorax of seven months' duration. Sputum 90 c.c. and always T.B. positive

The remote results, in the cases operated upon, are shown in Table IV. Of the 152 technically and clinically successful cases, 120 were bed cases and 32 were ambulant before operation; 146 cases had a positive sputum; in 6 it was negative. All these latter six were cases who had been under satisfactory pneumothorax, but the adhesions were contracting, causing an early expansion of the lung. These cases had been under observation for five years, and pneumothorax treatment was continued for at least two years during that time. Eight

more recent cases are still bed cases; 18 are ambulant and 126 are working; all have a negative sputum. All of the 19 technically unsuccessful, but clinically successful cases were bed cases, and all had tubercle bacilli in their sputum. Four years after operation, 7 are ambulant and 12 are working. All have a negative sputum.



Fig. 75.—Same case as Fig. 74. Five months later after severing many band adhesions, but there still remained an inoperable funnel adhesion which was electro-coagulated at its base. Cough and expectoration diminished. No positive sputum obtained in two years further observation.

In our series, we have operated upon five patients who were having uncontrollable hemorrhage from cavities in the lung which could not be collapsed because of adhesions. One of these patients had a bilateral pneumothorax. In four, a good lung collapse was obtained as a result of the operation, and bleeding ceased at once. In one case it was uncontrolled. The collapse was improved by operation in every case, and bleeding from the diseased lung was not aggravated.

TABLE IV  
INTRAPLEURAL PNEUMOLYSIS—REMOTE END-RESULTS OF OPERATION  
249 Cases

Result of Operation	No. of Cases	Condition Before Operation				Present Condition					Remarks
		Bed Amb.		Sputum		Bed Amb. Wk.*		Sputum			
				Pos.	Neg.			Pos.	Neg.		
Technically and clinically successful	152	120	32	146	6	8	18	126	..	152	Working 83%
Technically unsuccessful clinically successful.	19	19		19		..	7	12	..	19	Working 68%
Technically successful clinically unsuccessful	2	2		2	..	..	..	..	..	..	Two dead; 1 from Spon. Px. after Op.; 1 from hemorrhage opposite lung
Technically and clinically unsuccessful	76	62	14	76		This group comprised cases presenting adhesions unsuited for operation. In most cases minor adhesions of no technical importance were severed. All appropriate cases were subjected to other operative collapse procedures. The end result is not attributable to the pneumolysis—consequently not recorded here.					

\*Wk.—Working.

The technically and clinically unsuccessful group comprises 76 cases, of whom 60 were bed cases and 16 ambulant before operation. The sputum contained tubercle bacilli in all the cases. Inasmuch as all of these cases presented adhesions of a non-operable type, in combination with those which could be severed with safety, the end-results are in no way related to the operation, as the adhesions of mechanical importance remained untouched; these cases were submitted to other operative procedures, unless contraindicated, when the pneumothorax was continued.

### CONCLUSIONS.

Continuation of an unsatisfactory pneumothorax over a prolonged period is not justifiable because of the peril of disease extension to the opposite lung, to the gastrointestinal tract or to the larynx. Our experience covering the past twenty years and including approximately 1700 cases of artificial pneumothorax has demonstrated, during the past eight years, that intrapleural pneumolysis under thoracoscopic guidance will convert approximately 70 per cent. of unsatisfactory cases of pneumothorax into satisfactory ones. We have shown that less than 15 per cent. of recoveries take place as the result of the continuation of an unsatisfactory pneumothorax and that serious dangers attend the use of high intrapleural pressure in an attempt to stretch adhesions. If the adhesions prevent a satisfactory collapse of the lung after four to six months' trial, it is very improbable that a satisfactory end-result will be obtained by further continuation of the pneumothorax. After a test of this kind has been given, an unsatisfactory



pneumothorax should be converted into a satisfactory one by intrapleural pneumolysis. Should this be impractical, other surgical methods to obtain the desired results are advised.

Superiority of the electrosurgical method to the galvanocautery is unquestionable, and when properly executed, the operation is not dangerous. Our mortality, directly or indirectly due to operation, was 0.38 per cent. in 249 cases, including the use of both the galvanocautery and the electrosurgical method. Thus single operative mortality was only indirectly due to the operation.

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## CHAPTER XXI.

### OLEOTHORAX.\*

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**Terminology.**—The term "oleothorax" was applied by Bernou<sup>1</sup> in 1922 to the use of massive quantities of an antiseptic oil in the pleural cavity for therapeutic purposes, particularly for the treatment of pleuropulmonary fistula, especially those of the valve type, or in cases wherein the opening was small. Since Bernou's original publication, most of the work done upon oleothorax has been confined largely to France and to continental Europe. This method of treatment has received little attention in America. This lack of enthusiasm is, no doubt, due to conflicting reports regarding its efficacy, as well as an absence of detailed instructions regarding technic and definite information regarding indications.

Oleothorax was proposed by Bernou at a time when the possibilities of thoracic surgery had not gained a strong foothold in France; it was used therefore as a sort of "ultimum refugium" measure for the treatment of certain complications of pneumothorax therapy which we today know respond much better to other methods of treatment. This is particularly true of the treatment of pleuropulmonary perforation, collapse of rigid-walled cavities or cavities held expanded by adhesions, and in the treatment of certain types of empyemata.

**Indications.**—The generally accepted indications for an oleothorax are the following.

*First*, as a disinfection oleothorax for the treatment of certain types of pneumothorax empyemata.

*Second*, as an inhibition oleothorax (oleothorax antisymphysaire) to prevent expansion of the lung in threatened early obliterative pneumothorax wherein a satisfactory collapse cannot be maintained by air inflations, even though the inflation intervals have been shortened and the pressure has been increased.

If the oleothorax provides collapse to the diseased lung tissue only, it is termed an "elective" oleothorax.

*Third*, as a compression oleothorax to reestablish collapse in cases wherein air inflations properly carried out have failed to maintain a satisfactory collapse of the diseased lung tissue.

*Fourth*, stiffening of a labile mediastinum.

**Questionable Indications.**—The use of an oleothorax to combat the following conditions is questionable:

(a) The collapse of rigid-walled cavities or diseased lung tissue held expanded by intrapleural adhesions, wherein gas inflations, even under pressure, have proved ineffectual. For the relief of this condition far better results will

\*Thanks are due the publishers of the American Review of Tuberculosis for their courtesy in permitting the use of some of the illustrations and some of the material, particularly that referring to technic, which appeared in an article on Oleothorax, by the author, in Vol. XXV, No. 4, April 1932, American Review of Tuberculosis.

be obtained by an intrapleural pneumolysis. In the case of failure, one should consider a phrenic neurectomy or a thoracoplasty; an oleothorax should be resorted to only when an intrapleural pneumolysis and phrenic neurectomy fail, and a thoracoplasty is contraindicated or is unacceptable to the patient.

(b) An oleothorax has been recommended in place of a pneumothorax for patients who experience febrile reactions to gas, or pneumothorax patients in whom great difficulty is encountered in maintaining a proper collapse because of the rapid absorbability of the air. An oleothorax is contraindicated in the former for the reason that these febrile reactions are due to a sensitiveness of the pleura, and the introduction of oil in the place of air usually aggravates this condition and too frequently results in an exudate formation. If difficulty is encountered in maintaining a proper collapse on account of the rapid absorbability of air, much better results will be had by shortening the inflation interval rather than resorting to an oleothorax wherein the result will be questionable.

**Contraindications.**—Absolute *contraindications* for oleothorax are: (1) pleuropulmonary fistula with a large opening; (2) ordinary serofibrinous exudates complicating an artificial pneumothorax; (3) ordinary pneumothorax empyema which is tolerable, nontoxic and does not tend to chronicity; (4) as a substitute for a pneumothorax in patients who, for various reasons, are unable to undergo a prescribed course of pneumothorax therapy.

An oleothorax is contraindicated in the treatment of pleuropulmonary fistula with a large opening for the reason that the oil usually leaks through the fistulous tract, thereby not only adding to the discomfort of the patient by the continuous expectoration of oil, but also endangering him to an aspiration infection into healthy lung tissue, or even to suffocation.

In the treatment of pleuropulmonary perforation, even of the valve type, better results, and often excellent results, are obtained by the simple aspiration of air at intervals necessary to maintain a neutral pressure within the pneumothorax cavity.

In some cases of pleuropulmonary perforation of the valve type, the air accumulates so rapidly in the pneumothorax cavity that unless the patient is immediately relieved, death results in the course of a few hours, or even in a few minutes. In these cases, temporary relief is provided by the simple aspiration of air through an ordinary inflation needle, using a 100 c.c. syringe, or by connecting the inflation needle with a pneumothorax apparatus, the flow of which is reversed. Thus the quantity of air removed, as well as the rapidity of its removal, necessary to provide relief, can be accurately measured.

After having provided temporary relief, one should immediately insert a small trocar into the chest and through it introduce a small rubber catheter into the pneumothorax cavity. The catheter is connected to a length of rubber tubing, the distal end of which rests in a jar partly filled with water. Thus the air aspirated into the pleural cavity through the lung perforation escapes through the water, which serves as a check-valve, preventing a return flow of air into the pneumothorax cavity.

In still other cases, relief is brought about only by the continuous suction of air from the pneumothorax cavity at a uniform rate of speed. This is accom-

plished by partially exhausting the air of the jar which is partly filled with water, by means of a suction pump which is connected to a faucet, or any type of suction apparatus which can be carefully regulated. The rate of aspiration of air from the pneumothorax cavity should be so regulated that, above all, the patient is made comfortable. The pressure of the air in the pleural cavity can be accurately measured by observing a water manometer, which is connected to the tube leading from the chest, and should show slightly negative readings. This method of treatment has proved exceedingly efficacious in our hands. Under favorable conditions the treatment can be discontinued in the course of a few days, after which one resorts to simple aspiration of air at proper intervals until the perforation has closed. On the other hand, if the treatment has to be continued longer than a few days, it is important to withdraw the catheter every forty-eight to seventy-two hours and reinsert it at a new site, in order to prevent fistulization of the chest wall.

Oleothorax therapy is contraindicated in the treatment of the ordinary serofibrinous exudates complicating an artificial pneumothorax because the pleura being already inflamed is likely to respond to the introduction of oil with a purulent exudate which would only aggravate the situation. Oleothorax therapy should be embraced in pneumothorax therapy complicated by the presence of a serofibrinous exudate, only when this condition is associated with a chronic productive pleuritis which tends to early obliteration of the pneumothorax cavity. Under these circumstances, one may be forced to resort to an oleothorax in order to inhibit expansion of the lung, thus facing the danger of aggravating a condition already present by irritating a previously inflamed pleura.

Oleothorax is contraindicated as a substitute for pneumothorax therapy in patients who, for one reason or another, are unable to undergo the prescribed course of treatment for the reason that the oleothorax patient requires much more careful observation than is required in pneumothorax therapy.

*Preparation and Selection of Oil.*—As a base, two types of oil are used—mineral and vegetable; the first in the form of a paraffin oil and the second in the form of olive or Wesson oil. The oil is rendered antiseptic by the addition of gomenol in a strength varying from 1 to 10 per cent., depending upon the purpose for which it is to be employed. Both Küss<sup>2</sup> and Courcoux<sup>3</sup> add a small quantity of eucalyptol (about one-fifth the quantity of gomenol), believing that it makes the preparation more efficacious and less irritating.

**Gomenol.**—Gomenol<sup>4</sup> (*Niaouli oil*) is a volatile oil obtained by distillation of the leaves of a type of myrtle tree growing abundantly in the region of Gomen, New Caledonia. In its properties and composition niaouli oil closely resembles cajuput oil.

The toxicity and bactericidal properties of gomenol and its vapor have been studied very carefully. Baumetz and Main<sup>5</sup> studied the toxicity of gomenol by injecting a rabbit subcutaneously, using 4 Gm. of gomenol in an equal volume of olive oil for each kilogram of the animal's weight. They found that the animal presented no extraordinary phenomena.

Dubousquet-Laborderie<sup>6</sup> injected a dog subcutaneously with 6 Gm. per kilogram of the animal's weight, without obtaining any signs of intoxication.



**Bactericidal Properties.**—Clerc<sup>7</sup> studied the action of gomenol, as well as that of its vapor, with reference to its capacity to inhibit the growth of bacteria, and as a bactericide both *in vitro* and *in vivo*.

**Action in Vitro.**—Clerc exposed gelatine cultures inoculated with staphylococci to the vapor of gomenol and found colonies after 72 hours, but the colonies were small as compared with those in the control tubes. He also found that the vapor of gomenol inhibited very materially the growth of the human tubercle bacillus, but after nine weeks' exposure the vapor was not sufficient to destroy all organisms in the culture.

**Action in Vivo.**—In Clerc's animal experiments, in which he inoculated guinea-pigs with pure cultures of the tubercle bacillus, to which gomenol had been added, he found that the experimental animals lived very much longer than the controls. He injected tubercle bacilli into the pneumothorax cavity of rabbits carrying an artificial pneumothorax, after which he employed gomenol and found that it inhibited the development of tuberculous changes, and that tuberculous changes, when developing were much retarded and less severe than in the control animals.

**Antitoxic Action.**—In order to study the antitoxic influence of gomenol, Clerc used the toxin of the organisms of botulism, diphtheria and tetanus. He found that 10 times the fatal dose of botulinus toxin was completely neutralized by 0.5 c.c. gomenol.

As a result of his researches Clerc concluded that gomenol possesses a marked influence in inhibiting the growth of many microorganisms, and that this property is particularly pronounced toward the acid-fast group and less so toward the staphylococcus. The bactericidal power varies as against different organisms. The acid-fast organisms were killed in from five minutes to three hours, whereas, it required from three to nine hours to kill the staphylococcus. Clerc believes therefore that a concentration of 4 to 5 per cent. is sufficient in tuberculous empyemata, whereas the mixed-infection empyemata require a very much higher concentration (5 to 10 per cent.).

Gomenolized paraffin oil is recommended for all types of oleothorax, except in the treatment of a virulent mixed-infection empyema, in which event gomenolized olive oil or Wesson oil may be used.

In the inhibition oleothorax (*oleothorax antisymphysaire*), or elective oleothorax, and all cases in which a purulent exudate does not exist, either pure paraffin oil, or paraffin oil to which 1 per cent. gomenol has been added, is used. In Germany, jodipin, an iodized oil, is used in strengths varying from 2 to 10 per cent., in preference to gomenol. Diehl<sup>8</sup> has used jodipin in strengths as high as 40 per cent., and claims that it is well borne and without danger of iodism. One of the advantages of jodipin is the excellent contrast it provides on x-ray films.

**Disinfection Oleothorax.**—Paraffin oil, to which 5 per cent. gomenol has been added, is recommended for the nontoxic chronic pneumothorax empyemata. Paraffin oil, olive oil or Wesson oil, to which 10 per cent. gomenol has been added, is recommended as a disinfectant for those virulent and toxic types of pneumothorax empyema that are usually complicated by the presence of a

secondary infection. As already pointed out, gomenol, to be effective in these cases, must be used in strong concentrations; otherwise, it is unable to inhibit the growth of secondary invaders or kill them. One must be guided by personal experience in the selection of an oil, it being borne in mind that each oil possesses an advantage. Gomenolized paraffin oil is less absorbable and less irritating to the pleura than olive oil or Wesson oil. On the other hand, olive oil and Wesson oil not only possess great nutritive value, but, being more absorbable, allow the gomenol to penetrate deeper into the pleura. It is furthermore to be borne in mind that, whereas olive oil provides an excellent medium for the development of pyogenic organisms, it is reported that after extensive bacteriological studies bacteria will not propagate in paraffin oil.

If paraffin oil is used, it should be of standard make and correspond to the requirements of the *United States Pharmacopæia*.

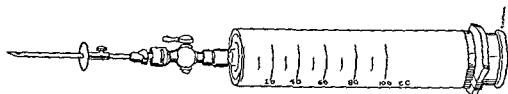


Fig. 1.—Illustrating syringe, one-way stopcock equipped with Luer lock, needle armed with guard and Luer lock. Equipment used in simple aspirations where the quantity of exudate is small, or in replacing air with oil.

If a vegetable oil is used, it must be of a high grade, chemically pure, and neutral in reaction. Wesson oil, which is a cottonseed oil closely resembling olive oil, is not only cheaper but is equally good.

In preparing the oil, it is customary to add the gomenol in the desired strength, and then allow the oil to stand for three weeks so that the two oils are thoroughly mixed. If paraffin oil is used, it is sterilized in its original container. One has only to uncap the bottle and withdraw about one-tenth of its volume. The neck is then stoppered with a small pledget of gauze or non-absorbent cotton and covered with rubber tissue. Olive oil can be poured from its original container into flasks and stoppered in a similar manner. The containers are then placed in an autoclave and sterilized by subjecting them to 30 pounds of steam-pressure for 20 minutes (275° F.), or 20 pounds steam-pressure for 30 minutes (260° F.). It will be found most convenient to keep the oil on hand in 100-c.c. containers. Once a container has been opened, it should be resterilized before using again.

**Syringes, Stopcocks, Needles, Adapters, Needle Guard.**—Three types of syringes are used: 2-, 10- and 100-c.c. When small quantities of oil are to be introduced into the pleural cavity for testing purposes, the 2- or 10-c.c. syringe is employed. The 100-c.c. syringe is used for handling large quantities of oil and for aspirating and irrigating purposes. The lumen of the 100-c.c. syringe tip should be of such diameter that exudates or oil can be aspirated or expelled easily. In our own work the syringe tip possesses a minimum internal diameter of 0.054 inch or 1.35 mm. All syringes except the 2-c.c., are equipped with Luer lock connections.

Three types of stopcocks are employed,—the one-way, three-way and four-way. The one-way stopcock is used in cases wherein small quantities of exudate are to be replaced with oil, and in all cases wherein a pneumothorax is being converted into an oleothorax. A turn of the stopcock valve prevents the aspiration of air or leakage of exudate or oil while the syringe is disconnected (Fig. 1).

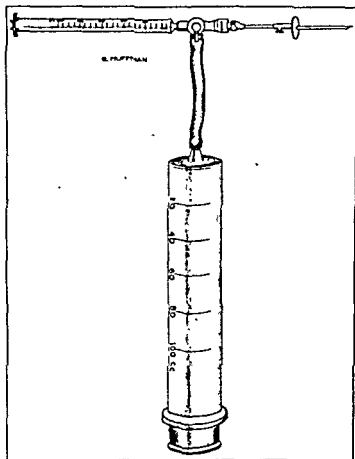


Fig 2.—Syringe equipped with three-way stopcock. Needle armed with guard. The barrel of an ordinary tuberculin syringe is slipped into the upper opening of the stopcock. The apparatus is used for measuring the pressure of oil in a compression oleothorax.

The three-way stopcock is used when one wishes to measure the pressure of oil in the oleothorax cavity, after a complete blockade has been accomplished. The lateral arm of the stopcock is connected with a 100-c.c. syringe by means of rubber tubing. The barrel of an ordinary 1- or 2-c.c. tuberculin syringe is inserted into the top opening of the stopcock (Fig. 2). The patient is placed recumbent in the dorsolateral position and the stopcock is held by an assistant in such a manner that the barrel of the attached syringe is vertical (Fig. 3). After having injected any given quantity of oil, one can readily estimate the pressure of oil within the pleural cavity by a turn of the stopcock which per-

mits the oil to flow up into the glass barrel. The stopcock is connected to the needle by means of a Luer lock.

The four-way stopcock is used in all cases wherein one wishes to aspirate large quantities of exudate or irrigate the pleural cavity. This stopcock is connected to a 100-c.c. syringe by means of a Luer lock. All arms of the four-way stopcock, except that leading to the syringe, are equipped with a valve. One of the lateral arms is used for ejecting exudate or irrigation solution into the discard flask; the other lateral arm is used for aspirating air into the

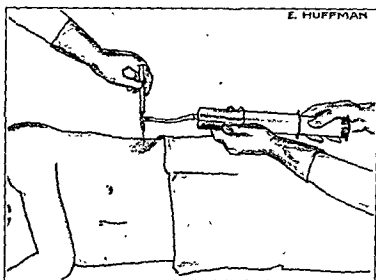


Fig. 3.—Illustrating method of measuring pressure of oil in compression oleothorax.

syringe in replacing exudate, or, when connected by means of a rubber tube to an irrigation solution container, one is enabled to aspirate irrigation solution into the syringe before injecting it into the pleural cavity. The four-way stopcock is connected to the needle by means of a short length of rubber tubing, at the end of which is a glass observation tube which fits to the needle by means of a Luer lock (Fig. 4).

The lumen of all stopcocks possess an internal diameter of 0.054 inch or 1.35 mm.

The needles now employed possess the following dimensions of lumen:

15 gauge needle	—0.054 inch or 1.35 mm.
14 " "	—0.063 " or 1.6 mm.
13 " "	—0.071 " or 1.8 mm.

The needles are of various lengths—from  $2\frac{1}{2}$  inches to 5 inches. The longer needles are equipped with an eye on the side,  $\frac{1}{8}$  inch from the point, and are used in cases wherein fibrin floccules are likely to occlude the needle, rendering aspiration difficult. All needles possess the Luer lock connection.

The 14 and 15 gauge needles are used in replacing air with oil in cases wherein one does not have to contend with an exudate. The 13 gauge needle is used in all cases wherein aspiration of exudate or lavage of the pleural cavity is to be accomplished.

**Needle Guard (Fig. 1).**—This guard fits all needles employed by us in our oleothorax work. The guard is first slipped upon the needle, which is introduced into the chest wall until it just penetrates the pleural cavity. The guard is then slipped along the needle until it fits tightly against the chest wall. A turn of the thumbscrew fixes it securely to the needle. The needle guard is then held firmly against the chest wall by an assistant, so that no matter what position the patient assumes during the course of aspiration or irrigation, there is no danger of the needle penetrating too deeply, thus puncturing the lung, or of the needle being accidentally withdrawn from the wall of the chest.

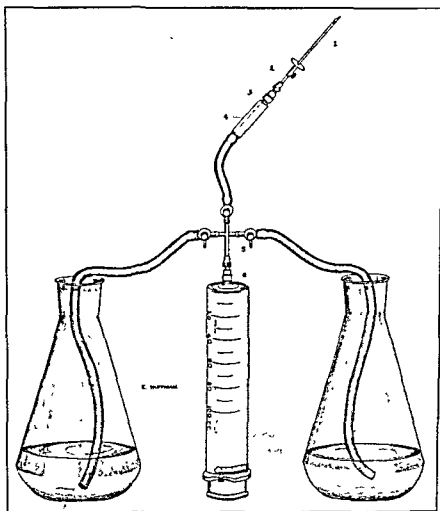


Fig. 4.—Illustrating equipment used for lavage of pleural cavity.

- |  |   |
|--|---|
| 1 13-gauge needle, 1.8 millimeter internal diameter. Eye on side near tip facilitates aspiration of exudates containing much fibrin. | 3. Luer lock.                                     |
| 2 Needle guard.  | 4 Glass observation tube equipped with Luer lock. |
|  | 5. Four-way stopcock                              |
|  | 6. Luer lock.                                     |

Flasks at either side hold irrigation solution or discharge materials

## TESTING THE SENSITIVENESS OF THE PLEURA.

A test of the sensitiveness of the pleura to oil is extremely important in all cases before attempting an oil blockade of the pleural cavity. This is particularly true in cases wherein one has to deal with a so-called virgin pleura, but it is of less importance when the oleothorax is employed for disinfection purposes.

A preliminary test of the sensitiveness of the pleura to oil is important for the reason that any foreign substance, even air, when injected into the pleural cavity is likely to provoke a reaction. In the presence of a purulent exudate, a preliminary test is usually not necessary for the reason that as a result of the inflammatory process already existing, the pleura has lost much of its sensitive-

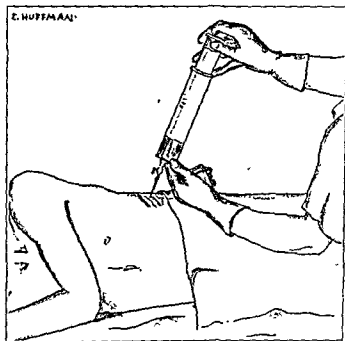


Fig. 5.—Position of patient in replacing air with oil.

ness. This is particularly true in those types of empyemata which are more or less chronic and associated with a chronic productive pleuritis.

In the beginning of our oleothorax work we employed rather large doses (10 to 20 c.c.) of pure paraffin oil, or 1 per cent. gomenolized paraffin oil as a first test dose, which was in accordance with the technic followed by Bernou,<sup>9</sup> Kuss,<sup>10</sup> Armand-Delille<sup>11</sup> and others. After having observed some very severe reactions, we adopted the plan of using small test doses, according to the manner described in a former publication.<sup>12</sup> The technic is as follows:

*Technic.*—As soon as it has been decided that air inflations are no longer efficient to maintain collapse of the diseased lung tissue for the desired length of time, we begin by injecting 1 or 2 c.c. of 1 per cent. gomenolized paraffin oil through the inflation needle into the pneumothorax cavity, after which the patient receives his regular inflation. A reaction to this dose rarely occurs. At the next regular inflation period, 4 c.c. are injected and inflation is carried

out as usual. Even though a constitutional reaction has been absent, a third test-dose is not made until one is certain, either by fluoroscopic examination or exploratory puncture, that an exudate is not present. If an exudate is present, it should be aspirated and the inflation carried out as usual, but oil injections are withheld until all tendency to exudate-formation has completely subsided. If there has been no intrapleural or constitutional reaction to the second test-dose, the third test-dose, consisting of 8 c.c. of oil, is injected through the inflation needle and followed by the usual inflation. If no reaction occurs to the third test-dose, we usually inject 15 or 20 c.c. of oil as a fourth test-dose at the next regular inflation interval. In the absence of a reaction, the quantity of oil

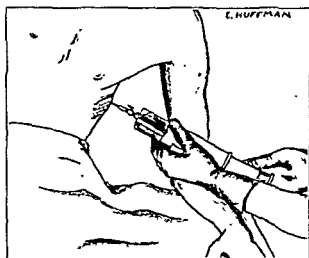


Fig. 6.—Illustrating method of aspirating pleural cavity when lavage is not required. The needle is inserted into the most dependent portion of the empyema cavity, preferably in the mid-axillary region.

injected at each subsequent sitting is usually doubled, up to an injection of 200 c.c., after which the dose is increased 100 c.c. at each sitting, but one should never inject more than 500 c.c. at one time. A very similar plan is followed by Kuss,<sup>2</sup> although he has no hesitancy in injecting 500 to 600 c.c. of oil at one sitting after one or two test-doses of 10 to 20 c.c. The conversion of a pneumothorax requiring more than 1500 to 2000 c.c. of oil in a man, or 1000 to 1500 c.c. in a woman, is not recommended. Ulrici<sup>13</sup> is much more conservative in his treatment, and does not undertake fillings of over 700 c.c., which is of course sufficient to blockade only a relatively small pneumothorax cavity.

If the regular gas intervals are more than one month apart, the test-doses up to 20 c.c. can be made at intervals of a week or ten days, but the patient should be confined to bed and carefully observed. Furthermore, one should always explore the pleural cavity to determine the presence or absence of an exudate before making further injections, after the second or third test-dose has been administered. If this rule is followed in every case, one will be spared the embarrassment of suddenly finding that a purulent exudate has developed unrecognized.

In making the exploratory puncture, the patient is placed recumbent in the dorsolateral position (Fig. 5); the needle is then inserted into the most dependent portion of the pneumothorax cavity, after which the patient is seated upright and aspirated, using a 50-c.c. or 100-c.c. syringe (Fig. 6). An exudate, if present, occupies the lower level and the oil, being of a lighter specific gravity, floats on top. The fluoroscopic examination gives little or no information concerning the presence or absence of an exudate, in the presence of oil, for the



Fig. 7.—Radiograph showing two fluid levels. The lower, denser shadow is due to a purulent exudate (level indicated by lower arrow). The upper shadow is due to gomenolized oil. Upper arrow indicates lateral chest-wall adhesion.

reason that the eye is not sensitive enough to differentiate the oil from exudate strata on the screen. By means of a good radiograph, one is able to recognize a purulent exudate beneath the overlying oil because of the difference of density of the two shadows (Fig. 7).

There is no way of telling beforehand what the reaction of the pleura will be to the test injection. If the pleura proves to be extremely sensitive to the gomenolized oil, one might try paraffin oil, which is perhaps less likely to produce reactions and is equally efficient, except when the oil is to be used for disinfectant purposes. The only advantage of the gomenolized oil is that it is antiseptic.



It is generally believed that a recently inflamed pleura is more sensitive than one which has not been the site of an inflammatory process, but this is not in accordance with our experience. In one of our cases (Fig. 8), in which the patient had a recent exudative pleuritis, we replaced 300 c.c. of air with 300 c.c. of 1 per cent. gomenolized paraffin oil at the first sitting, and there was no reaction. On many occasions we have replaced 100 to 250 c.c. of air with paraffin



Fig. 8—Elective oleothorax which has remained undisturbed for more than five years. Patient has been leading an ordinary life for three and one-half years.

or gomenolized paraffin oil at the first sitting, without reaction. This experience is in accordance with that of Diehl,<sup>14</sup> who aims to fill the pleural cavity as completely as possible, even at the first sitting, believing that reactions are much less common by this method. On the other hand, Morin and Bouessée<sup>15</sup> report a striking number of complications in a material consisting of 60 cases. They

advise gradually increasing quantities of oil and recommend at least six months in attaining a complete filling of the pleural cavity.

In many of our cases which were rapidly converted without reaction, there had been a recent exudative pleuritis, and in other cases there was no evidence of a previous inflammatory process in the pleura. While it is our custom to occupy two or three months in the conversion of a pneumothorax into a complete oleothorax, we have also, with perfect ease and without reaction, converted other cases within a period of one or two months. In one of our cases, 1950 c.c. of air were replaced with oil in one month. In another case, 1680 c.c.

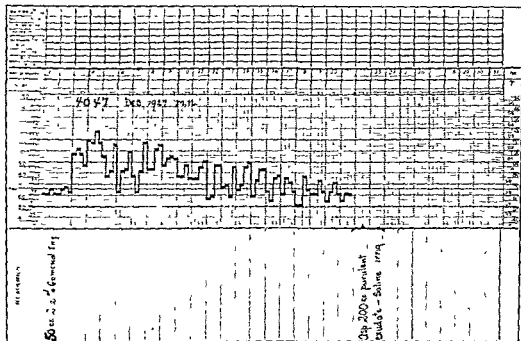


Fig. 9.—Chart showing severe febrile reaction to injection of 50 c.c. gomenolized paraffin oil, in a patient who had already received two smaller test doses without reaction. The exudate formation ceased completely after a single aspiration and irrigation.

of air were replaced with oil in two months, both without complications or reactions.

**Reactions.**—The reaction of the pleura to the introduction of oil, air or any other foreign substance is extremely variable, even in the same individual, and probably depends upon its irritability at the particular time the injection or inflation is made. What factors bring this about are not known, but abundant proof of this statement exists in the sudden occurrence of a pneumothorax pleurisy, with or without exudate formation, following air inflation or oil injection, in patients in whom all factors related to the treatment were essentially unchanged, *i. e.*, the interval, quantity of air or oil used, initial and final pressure, etc.

Reactions to oil, like air, are likely to occur at any phase of the treatment. In many of our cases we observed no reaction to the preliminary test dose, nor to

the gradually increased doses, until we had reached a dose of 50 or 100 c.c. (Figs. 9 and 10). As already stated, in a case of a recent exudative pleuritis, we replaced 300 c.c. of 1 per cent. gomenolized paraffin oil at the first sitting without reaction of any type, after which a complete blockade of the pleural cavity was rapidly established and has been maintained without reaction since April, 1928—now over five years (Fig. 8).

In another case, wherein a pneumothorax pleuritis associated with exudate formation had recently existed, 150 c.c. of air were replaced with 150 c.c. of

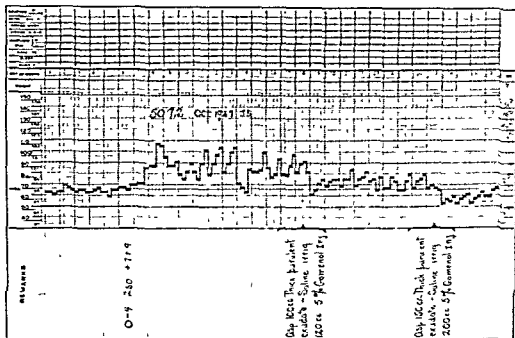


Fig. 10.—Chart showing febrile reaction associated with exudate formation after 50 c.c. injection of 1 per cent. gomenolized paraffin oil. The patient had not reacted to test doses. The exudate formation disappeared in a few weeks, after which a complete oil blockade was successfully established.

paraffin oil at the first sitting without reaction. An oil blockade of the pleural cavity was rapidly established and has been maintained without complication since November, 1927—now nearly seven years (Figs. 11 and 12).

On the other hand, in another case, a single injection of 5 c.c. of gomenolized paraffin oil produced an exudative pleuritis which persisted for more than a year. In still another case, a preliminary test injection of 2 c.c. of 1 per cent. gomenolized paraffin oil produced marked toxic phenomena; the patient complained of "grippy" sensations and nausea, but no vomiting; the temperature was elevated one degree. After three days, during which time the patient complained of feeling "sick all over," the symptoms subsided. Two weeks later, a fluoroscopic examination revealed a small quantity of exudate occupying the costophrenic angle, which, upon aspiration, proved serous in character.

It is a curious fact that in some cases the oil proved intensely irritating to the pleura and caused an exudate formation, but that this complication subsided with the continuation of the same irritant. In one case 100 c.c. of air were replaced with 100 c.c. of paraffin oil at the initial sitting. Twenty-four hours later there was a febrile reaction which mounted to 101.2° F. and lasted

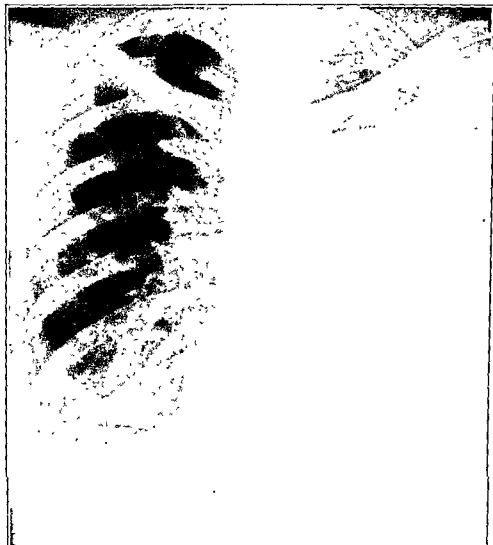


Fig. 11—Case 3870—March, 1928. Radiograph showing oil blockade of pleural cavity to inhibit expansion of the lung in case of threatened obliterative pneumothorax.

for one day. One week later a similar treatment was administered—within twenty-four hours the patient experienced a chill lasting two hours, after which the temperature mounted to 100° F. This febrile reaction persisted, reaching 102° F. on the fifth day, after which it quickly subsided. One week later 250 c.c. of serous exudate were removed and 100 c.c. of gomenolized oil injected—there was no reaction. During the course of the next two months the patient received a total of 1200 c.c. of gomenolized oil without reaction of any type. The

patient then disappeared from observation. Two years later she again presented herself and reported that the oil had remained undisturbed and that meanwhile she had experienced no reaction or discomfort of any sort. An exploration of the pleural cavity revealed clear oil but no exudate.



Fig 12—Case 3870—February, 1933. Radiograph of same case as Fig. 11. An inhibition oleothorax has been maintained uncomplicated for more than six years. The oleothorax has been in the course of withdrawal for the past two years. The patient has been leading an ordinary life for two and one-half years.

It should be stated that in the beginning of our oleothorax work, we, like most of our colleagues, used massive quantities of oil with surprisingly few reactions, and it was only after the occurrence of severe reactions in a few cases, as well as the published accounts of the experience of others, that we realized the danger of this technic and resorted to our present conservative method

Once a reaction occurs it should be allowed to subside completely before further injections of oil are made, and one should then begin with extremely small doses. If, at any time, an exudate formation occurs, one should aspirate the exudate and withhold further oil injections until all tendency to exudate formation has subsided. If the exudate tends to persist in its formation, it is

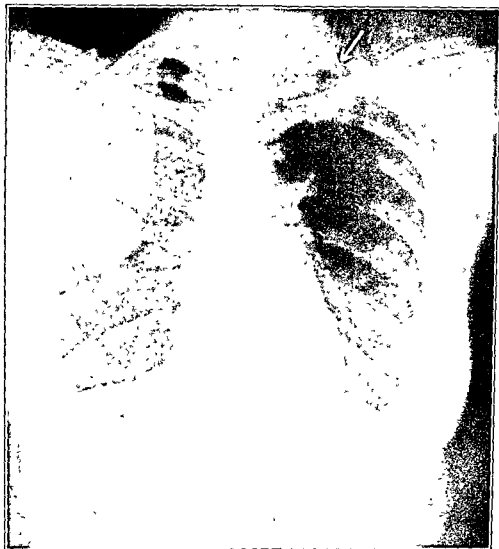


Fig. 13.—Case 5352—February, 1931. Uncomplicated elective oleothorax right successfully maintained for more than two years, after having four times failed because of the development of a purulent exudate. Fresh excavation in left upper indicated by arrow.

no doubt better to abandon the oleothorax temporarily by aspirating all exudate and oil. Then, after all tendency to exudate formation has subsided, one can attempt to reestablish the oleothorax.

In several of our cases, we were successful in converting a pneumothorax into an oleothorax only after two or three failures, and in one case we succeeded in establishing an oil blockade only after having failed four times (Figs. 13 and 14).

In spite of the fact that early in our work we were eminently successful in rapidly establishing a satisfactory oleothorax without complications in a large number of cases, using rather massive quantities of oil, we now feel this method of conversion is dangerous and it is much better to take three or even six months in the conversion of a pneumothorax into an oleothorax rather than to face the danger of complications or failure because of too rapid conversion.



Fig. 14—Case 5352—February, 1933. The same case as Fig. 13—Two years later, the elective oleothorax has remained undisturbed and uncomplicated. Pneumothorax left for more than two years. Excavation apparently closed.

*Classification of Reactions.*—Reactions are classified as (1) intrapleural and (2) constitutional. Intrapleural reactions consist of (a) pain, and (b) exudate formation. The pain is of the characteristic pleuritic type, involving the entire hemithorax, and is usually followed very quickly by an exudate formation. The exudate formation may be serofibrinous, seropurulent or purulent, and may develop without pain or constitutional symptoms, although as a rule it is asso-

ciated with fever. All exudates are usually serofibrinous to begin with. If the reaction is severe, the exudate generally rapidly becomes first seropurulent and then purulent. Exudates which are destined to become purulent are commonly associated with a marked constitutional reaction—high fever and severe pain. However, we have seen cases wherein the purulent exudate was discovered accidentally, having developed without any constitutional disturbance. It is for this reason that one should always explore the oleothorax cavity before making a fresh instillation of oil.

*Fever* is the most frequent constitutional symptom and may be the only symptom. A febrile reaction may follow within a few hours after the instillation of oil. The elevation of temperature may be moderate, around 100° F., or more marked, arising from 101° to 102° F. within a few hours and subsiding within the course of a few days. Reactions of this type may not be attended by an exudate formation.

In another group of cases, the febrile reaction is more severe—the temperature rising to 102° or 103° F. within a few hours (Fig. 9). These patients frequently describe themselves as being "sick all over" which condition they may attribute to an acute attack of "grippe." The patient looks extremely ill, the features are pale, prostration is marked, and there is a total anorexia. Chest symptoms, pain and exudate may or may not be present in the beginning. These cases almost invariably develop an exudate which is usually purulent in character.

In still another group of cases, a febrile reaction may make its appearance at the end of a week or ten days, after which the temperature gradually rises, reaching 101° to 103° F. in a few days. In cases of this type, an exploratory puncture of the pleural cavity invariably reveals an exudate—usually seropurulent or purulent in character.

Reactions occur in approximately 50 to 60 per cent. of all cases wherein an attempt is made to establish an oleothorax for the purpose of inhibiting expansion of the lung or as a compression oleothorax. In our first series, 54 per cent. of our cases developed an exudate—of these, 24 per cent. became purulent. Sixty per cent. of the purulent exudates "cleared up" so that we were later able to reestablish the oleothorax. But in the remaining cases we were forced to abandon the oleothorax permanently.

### PNEUMOTHORAX PLEURITIS.

A discussion of oleothorax would not be complete without at least some reference to the most important factor rendering this form of treatment indicated. Pneumothorax pleuritis is perhaps the most frequent complication of pneumothorax therapy and occurs, in at least minor degrees, in the vast majority of cases. It may be mild and productive of no symptoms, and recognized only by a careful roentgenological study of the pneumothorax cavity, as a result of which one may discover a few cubic centimeters of exudate occupying the costophrenic angle. Or it may be severe and associated with marked constitutional disturbance, fever, etc. In these cases the exudate forms rapidly.

Pneumothorax pleuritis is most common in cases complicated by the presence of pleuritic adhesions. It may occur at any phase of the pneumothorax therapy,



either after the first few inflations or later, after the pneumothorax has long been established.

Pneumothorax pleuritis is due to a variety of causes, the most common of which are the introduction of a foreign substance into the pleural cavity, the separation of adhesions, the trauma induced by inflation, the changes produced in the intrapleural pressure, the temperature of the inflation material, etc.

Pneumothorax pleuritis is an inflammatory reaction to irritation, and is mild or severe, depending upon the sensitiveness of the pleura. The reaction varies in intensity from a mild hyperemia with little or no exudate formation to a very high degree of inflammation associated with abundant exudate formation, which may be serofibrinous, seropurulent or purulent.

Strictly speaking, pure serous inflammations of the pleura do not exist since small accumulations of fibrin, either upon the surface of the pleura or in the exudate, are present in all cases. The exudates naturally vary from an almost pure serous exudate containing little fibrin to those wherein much fibrin is present. Nevertheless, these exudates must all be considered serofibrinous. The purulent exudates are rarely purulent to begin with. In most cases the exudate is serofibrinous in the beginning, but it becomes rapidly transformed into first a seropurulent and then a purulent exudate. In these cases the pleura itself is the site of a high grade inflammatory process; the blood-vessels are engorged and the lymph-vessels are dilated and filled with leukocytes. The deposits on the pleura are mostly fibrinous. In a purulent exudate the leukocytes appear very quickly in the free fluid as well as in the fibrin masses. Through the proteolytic ferments, which arise through the destruction of the leukocytes, a greater portion of the fibrin is dissolved, the exudate then becoming pure pus and more fluid. The action of the proteolytic ferments in digesting fibrin facilitates evacuation of the exudate, which otherwise has a tendency to block the aspirating needle.

If a purulent exudate exists for a long time, the lymph passages undergo an obliterating inflammation which prevents resorption of the exudate. Such exudates are likely to exist under high pressure, and it is under these circumstances that a lung perforation is most likely to occur.

The exudates which are mostly serous may resorb completely in a few days or weeks; exudates rich in fibrin require more time but a complete resorption can take place if the fibrin is dissolved through the action of ferments. If an exudate persists for a long time, the inflammatory process assumes a reparable character; the fibrin exercises a chemotactic action upon the connective tissue and the blood-vessels of the underlying pleura, bringing about the formation of a vascular granulation tissue which grows out of the pleura into the fibrin, producing a "chronic productive pleuritis."

Obliteration of the pneumothorax cavity is brought about through adhesion of the two pleural sheaths. This process usually begins at the lowermost part of the pneumothorax cavity and progresses from below upward until eventually a total synechia of the two pleural sheaths has taken place. If the obliterative changes occur slowly, a satisfactory pneumothorax may be maintained, but if they are rapidly progressive, the lung will expand and attach itself to the chest

wall long before the proper period of pneumothorax treatment has been carried out. An early obliterative pneumothorax can at times be prevented by more frequent inflations or increased pressure, but if under these circumstances a satisfactory collapse cannot be maintained, an oleothorax is indicated. If an uncomplicated complete oil blockade of the pleural cavity is established, expansion of the lung is inhibited because of the incompressible nature of the oil employed. Unfortunately, in far too large a number of cases, a successful blockade cannot be established because of the irritating influence of the oil upon the pleura, resulting in exudate formation which only aggravates the condition we are striving to prevent.

From what has already been said, it must be apparent that an oil blockade of the pleural cavity should be undertaken only when one is convinced that a satisfactory collapse cannot be maintained by air inflations, even though one materially shortens the interval and, if necessary, resorts to higher pressure.

#### INHIBITION OLEOTHORAX (OLEOTHORAX ANTISYMPHYSAIRE).

This type of oleothorax is established for the purpose of inhibiting expansion of the lung when the collapse cannot be maintained by air inflations, even though the intervals have been shortened and higher gas pressures have been resorted to (Figs. 11 and 12).

#### ELECTIVE OLEOTHORAX.

An oleothorax which lies only over the diseased lung portion is designated as an "elective" oleothorax (Figs 8, 13, 15). It is particularly indicated in those cases wherein a selective collapse has been established but cannot be maintained on account of the tendency of the lung to expand even under the increased gas pressure. An elective oleothorax is established only after the healthy lung tissue has expanded and attached itself to the chest wall. Since this process of adhesion of the lung to the chest wall usually begins below and extends upward, one establishes the elective oleothorax only when the expansion and adhesion process has reached the level of the diseased lung tissue. If the pleura over the healthy lung tissue possesses little tendency to become adherent, adhesion of the two pleural sheaths may be effected by the injection of small quantities of oil sufficient to irritate the pleura, which will be followed by an adhesion formation, after which an oil blockade is established.

An elective oleothorax is especially well borne and acts similarly to an extrapleural paraffin implantation, with the exception, however, that one is dealing with a liquid medium which may be aspirated and replaced at will. Perforation seldom, if ever, takes place; the fluid usually remains clear and complications are seldom encountered once a satisfactory blockade has been established. Unquestionably, our most gratifying results have been obtained in cases wherein an oleothorax of this type was established.

An elective oleothorax is particularly serviceable in bilateral types of disease wherein it is desirable to effect and maintain a collapse of the diseased lung tissue only (Figs. 13, 14, 15, 16).

## COMPRESSION OLEOTHORAX.

Whereas an inhibition oleothorax is established for the purpose of maintaining collapse, a compression oleothorax is used to reestablish collapse. It is therefore particularly indicated in those cases wherein the lung has partially expanded, as a result of a progressive symphysis of the pleura, or the traction of



Fig. 15.—Case 3520—December, 1929. Elective oleothorax right. Productive type of tuberculosis with excavation left upper. A left phrenic neurectomy was performed January, 1927.

gradually thickening adhesions which cannot be severed by means of an intrapleural pneumolysis. Frequently, in cases of this type, a pneumothorax pleuritis with persistent exudate formation has rendered the maintenance of a satisfactory collapse impossible, the lung having been partially expanded beneath the exudate. A compression oleothorax has been recommended by some authors for the collapse of rigid-walled cavities, or diseased lung tissue which is held expanded

by adhesions. In accordance with our experience, and that of many other observers having had extensive experience, a compression oleothorax is of doubtful value in these cases; there is furthermore the great danger of a lung perforation, if the oil blockade is established under pressure

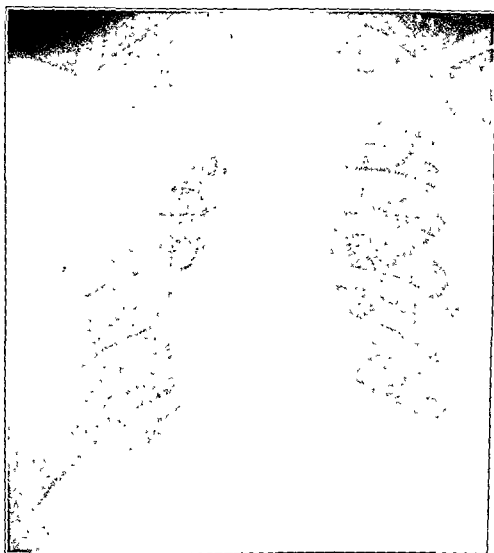


Fig. 16.—Case 3250—February, 1933. Radiograph of same case as Fig. 15. The elective oleothorax right has remained undisturbed and uncomplicated for more than four years. Phrenic neurectomy left six years ago. Note rise of diaphragm, large gas bubble in stomach and dense fibrosis with disappearance of excavation.

**Technic.**—After having determined by means of preliminary test-doses that the oil will be tolerated by the pleura, a complete blockade of the pleural cavity is accomplished in the following manner: The patient is placed recumbent in the dorsolateral position, lying on the healthier side (Fig. 5). A small cushion is placed in the axillary region so that a bulging of the chest is produced. A 13-gauge needle, armed with a one-way stopcock, is then inserted in the axillary

region at the highest point of bulging. If small quantities of oil are to be injected, a 10-c.c. or 50-c.c. syringe is used. Otherwise, a 100-c.c. syringe is filled with oil, warmed to a point so that it will be delivered inside of the pneumothorax cavity at body temperature. Oil which is too cold or too hot is likely to provoke a reaction. Furthermore, warming of the oil facilitates injection by rendering the oil less viscid. After having connected the syringe with the stopcock, the valve is opened and 20 c.c. of 1 per cent. gomenolized paraffin oil is injected into the pleural cavity. The piston is then withdrawn, aspirating an equal volume of air into the syringe. This maneuver is repeated until the syringe has been emptied of oil and replaced with air. In this manner the desired quantity of oil is introduced to replace air which has been aspirated. The syringe is then disconnected from the stopcock, and the latter is connected by means of an adapter to the pneumothorax apparatus. The stopcock valve is next opened and air, sufficient to bring the intrapleural pressure up to neutral, is allowed to flow into the pneumothorax cavity.

The injection of oil and the aspiration of air in units of 20 c.c. is recommended in order not to disturb the intrapleural pressure greatly; otherwise, a severe febrile reaction might result. Furthermore, if the oleothorax is nearing completion, the injection of 100 c.c. of oil at one time may bring about marked pressure phenomena, even causing a perforation into the lung if an area of softening exists in the pleura. It has already been stated that the quantity of oil injected is usually doubled at each sitting, but one should never exceed a dose of 400 c.c. to 500 c.c. in the adult male, or 300 c.c. to 400 c.c. in women.

After many sittings of this sort, or when the oleothorax has been nearly completed, a fluoroscopic or radiographic examination of the patient in the erect position will show a small bubble of air at the top of the pneumothorax cavity. At the next sitting this bubble is easily aspirated and replaced with an equal quantity of oil. The oleothorax is thus complete.

The technic of an elective oleothorax is similar to that described above except that since a much smaller pneumothorax is being converted into an oleothorax, one works with smaller quantities of oil in completing the blockade. Rarely more than 100 c.c. are used as a maximum dose at one sitting.

The technic employed in a compression oleothorax is identical to that of an inhibition oleothorax, except that the pleural cavity should be prepared for the high oil pressures by means of preliminary high air pressures; otherwise, there is great danger of inducing a pleural reaction or bringing about a lung perforation. If, therefore, one contemplates the establishment of a compression oleothorax, the intrapleural pressure should be gradually elevated by air inflation before a complete oil blockade of the pneumothorax cavity has been affected, after which one can safely proceed with the injection of oil under pressure. Needless to say, this procedure must be carried out with great caution.

Many devices have been proposed for the measurement of the pressure under which the oil exists in the pleural cavity, none of which are entirely satisfactory or accurate. Early in our work we were guided solely by the resistance encountered in pressing the syringe piston, and we still feel that the sense of touch to the experienced hand is a most excellent and dependable guide. During recent

years we have used a device, already described, (Fig. 2) which is a useful adjunct inasmuch as one is enabled to measure and record the pressure under which the oleothorax exists.

If the compression oleothorax is maintained under much pressure, it is important that the needles used in the injection should not exceed a 15-gauge which possesses an internal diameter of 0.054 inch, or 1.35 mm. Otherwise, oil is almost sure to escape from the pleural cavity into the surrounding structures, producing a paraffinoma. This complication can be avoided by inserting the needle in an oblique direction, and, after withdrawal, covering the puncture site with a small pledget of gauze, upon which one places one or two one-inch squares of rubber sponge, about one-third inch thick, followed by a tight strapping of the chest with adhesive tape.

Many cases wherein a compression oleothorax is indicated are complicated by the presence of a labile or lax mediastinum, which must be overcome before compression can be exerted.

**Oil Replacement.**—Since every type of oil is absorbable to some extent, and this depends largely upon the permeability or absorptive capacity of the pleura in the individual case, as well as the type of oil used, oil replacements are necessary from time to time in order to maintain collapse. While no definite rule can be followed in making oil replacements, once a satisfactory oil blockade has been established, the pleural cavity should be explored at intervals of at least once a month during the first few months; at this time one should also determine the presence or absence of an exudate and be prepared to make an oil replacement. With this in view, the patient is placed recumbent in the dorsolateral position (Fig. 5). A 13-gauge needle, armed with a three-way stopcock, is inserted into the most dependent portion of the oleothorax cavity. This point is readily established by direct finger palpation, by which one can determine the absolute line of demarcation between the flatness of an oil blockaded pleural cavity and the abdominal tympany or liver dullness. After having introduced the needle, the patient is seated upright or inclined in such manner that the aspiration of an exudate, if present, is facilitated (Fig. 6). It should be remembered that an exudate, being heavier than oil, always occupies the lowermost portion of the pleural cavity. If an exudate is encountered, one should aspirate until pure, clear oil is recovered. Further injections of oil should be withheld until the tendency toward exudate formation has ceased. If the exudate formation tends to persist, it may be necessary to abandon the oleothorax temporarily, or even permanently. If no exudate is present, the patient is returned to the recumbent position and the syringe is disconnected, filled with oil and again connected with the stopcock, which is equipped and held as illustrated in Fig. 3. A test of the pressure under which the oil exists is then made by turning the stopcock upward. If the oil is under pressure, it will rise into the glass gauge, the amount of pressure being determined by the elevation to which the oil rises. If the oil is not under pressure, the stopcock should be turned down at a right angle to the needle, thus closing the passage leading to the oil gauge and opening that leading to the syringe. The oil, which is warmed to a proper temperature, is then slowly injected into the pleural cavity by gentle pressure upon the syringe piston. If

the oleothorax is being maintained at a "neutral" pressure, the injection should be stopped as soon as one encounters resistance, which, according to Bernou<sup>18</sup> indicates the limit of expansion of the pleural cavity.

If the oleothorax is being maintained under pressure, one should make a test of the pressure under which the oil exists following the injection of each 5 c.c. of oil, after resistance is encountered in pressing the syringe piston.

The injection of 100 c.c. of mineral oil at monthly intervals may suffice to maintain collapse during the first few months of an oleothorax, after a complete blockade has been established. Later on the absorptive capacity of the pleura decreases, owing no doubt to a moderate thickening which gradually develops. Thus smaller quantities of oil have to be replaced. At the end of the first year, perhaps not more than 10 to 40 c.c. of oil, at intervals of three or four months, will be found necessary.

**Withdrawal of an Oleothorax.**—After an oleothorax has been maintained for a relatively long period of time (two years or more), it will be found that replacements are seldom, if ever, necessary. Consequently, the oil is permitted to remain undisturbed until one feels that the oil can be safely withdrawn and the lung reexpanded. In this matter one is guided by the same rule as that applied to pneumothorax therapy, except that in the latter the absorption of air brings about expansion of the lung, whereas, the oil being very slightly absorbable, has to be withdrawn.

When the oleothorax has been maintained for the purpose of inhibiting an early obliterative pneumothorax, Bernou<sup>18</sup> believes that if the oleothorax has been well established for a few months, one may evacuate the oil and resort to air inflations. In our opinion, this is not a wise procedure, especially if the oleothorax is well borne, since obliterative changes, once started, are usually progressive. Consequently, if air inflations failed to inhibit the expansion of the lung at one time, there is little reason to believe that they would later be successful.

Once it has been decided that the oleothorax has served its purpose, the lung should be reexpanded by the withdrawal of small quantities of oil at regular intervals, over a period of time sufficient to convince one that the lung lesion remains healed. If the oleothorax has been maintained over a period of several years, a year or more should be occupied in its withdrawal.

In the case of a small elective oleothorax, which is well tolerated, we feel that the oil can be left indefinitely undisturbed with far less danger of complications than is encountered in an extrapleural paraffin implant of equal volume.

**Labile Mediastinum.**—Air inflated into the pleural cavity naturally exerts its greatest influence at the point of least resistance. Since adhesions almost invariably exist, at least to some extent, between the diseased lung tissue and chest wall, and offer more or less resistance, a lax or labile mediastinum, being the point of least resistance, responds to air inflations by bulging long before a satisfactory collapse of the diseased lung has been accomplished (Fig. 17). In cases of this type the pneumothorax cavity should be explored by means of the thoracoscope, even though adhesions have not been visible upon the radiograph. If this is done, one is usually rewarded by the discovery of adhesions of

technical importance, and a satisfactory collapse can usually be established following their separation by means of an intrapleural pneumolysis. In other cases the physical examination, as well as stereo-radiographs, will reveal that the diseased lung is densely adherent over a widespread area. Under these circumstances, or if the pneumolysis fails, one should attempt to thicken and stiffen

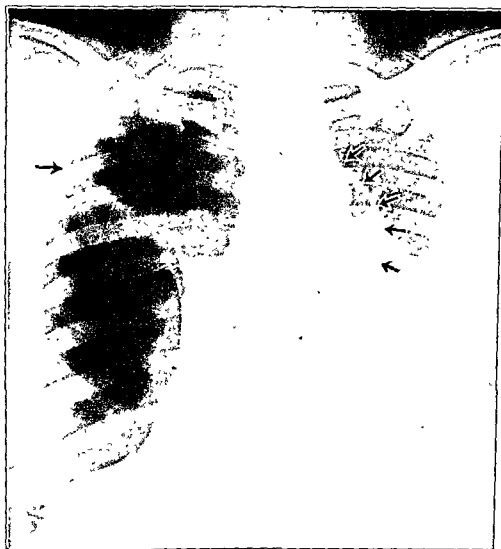


Fig 17.—Bulging of the mediastinum to left, indicated by arrows. Note downward displacement of diaphragm and lateral chest-wall adhesion right, indicated by arrow. See text, "Labile Mediastinum."

a labile mediastinum by inducing slight pleural reactions which are localized to the bulging area. The technic is as follows: The patient is placed either recumbent in the dorsolateral position and the injection needle introduced in the second or third interspace close to the sternum, or semi-prone in the recumbent position and the needle introduced in the third or fourth interspace anterior axillary line. In either position the needle should be so introduced that it just



penetrates the pneumothorax cavity; 5 to 10 c.c. of 1 per cent. gomenolized oil are then slowly injected and permitted to flow down the anterior chest wall into the bulging mediastinum (Fig. 18). The patient should remain in this position for one or two hours in order to permit a localized action of the oil, after which a 13-gauge needle is inserted into the lowermost portion of the pneumothorax cavity. The patient is then seated upright in such a position that



Fig 18—Radiograph of patient recumbent in dorsolateral position. Note marked bulging of mediastinum filled with radio-opaque oil, indicated by arrows.

the oil will flow into the most dependent portion of the pneumothorax cavity. The oil is then aspirated and the lowermost portion of the pneumothorax cavity washed with saline solution, until all evidence of the oil has been removed. Subsequent injections are carried out at intervals of a week or ten days, with slightly increased doses. After the desired effect has been accomplished, one can then proceed with an oil blockade of the pleural cavity under pressure.

## OLEOTHORAX AS A SUBSTITUTE FOR PNEUMOTHORAX WHEN FEBRILE REACTIONS FOLLOW AIR INFLATION.

Oleo thorax therapy has been applied successfully in some cases in which air inflations have been attended with severe febrile reactions. But satisfactory results have been obtained in so few cases that undoubtedly it is better to resort to other methods of treatment—phrenic neurectomy, etc.

### DISINFECTION OLEOTHORAX.

*Mode of Action of Oleo thorax in Empyema.*—The fundamental principle of a disinfection oleo thorax is that, after a complete removal of the pus and a thorough irrigation of the pleural cavity, the oil injection should be massive, and sufficient to bathe the entire surface of the serosa. According to Bernou<sup>16</sup> the beneficial influence of a disinfection oleo thorax is not to be attributed entirely to its antiseptic properties but perhaps even more to its proteolytic activities. Sergent and Turpin<sup>17</sup> attribute the beneficial influence of gomenol to its ability to irritate the pleura rather than to its disinfectant or bactericidal powers. In these cases, the oil acts as an irritant, which stimulates an inflammatory reaction, characterized first by congestion of the pleura and followed by an abundant migration of polynuclear leukocytes. The destruction of the polynuclear leukocytes releases proteolytic ferments, which liquefy the products of caseation, thus permitting a cleansing of the pleural wall.

The proteolytic action is not the only action of a disinfection oleo thorax. There is also a lipolytic ferment action. The presence of lipases is revealed by the saponification of oil removed from the pleural cavity. Oil which has undergone saponification presents a characteristic opaque appearance.

According to Bernou one must assume a direct action of the lipases upon the waxy capsule of the tubercle bacillus, similar to that obtained *in vitro*. The absorption of these lipases with the oil by the lymphatics permits a deeply penetrating action. It is possible that these lipases, having been absorbed, are able to elevate the percentage of the lipase in the blood, which is ordinarily diminished in the tuberculous individual. This increase of the lipolytic power of the blood might permit a disintegration of the waxy capsule of the tubercle bacillus, bringing about a liberation of the intracellular antigen, which, in turn, stimulates an active immunity against infection. Bernou claims that in many cases he has observed that the resorption of the oil was accompanied by strongly lipolytic reaction.

The experiments of Binet and Verne prove that the injection of the lymphatics with the oil and fatty acids creates, without doubt, an unfavorable soil for the development and propagation of tubercle bacilli. It is possible, too, that this momentary occlusion also limits the resorption of toxins and might partially explain the rapid amelioration of symptoms and rapid improvement of the general health which sometimes follows the institution of an oleo thorax. These results are not always evident because the resorption of oil in a thickened pleura is rapidly diminished or practically nil.

Another favorable effect of the lipases is the liberation of the gomenol which results from the saponification of the oil and the disintegration of the

acid molecule. This rapid liberation of gomenol probably allows a massive antiseptic action, which is more efficient on the pleura, causing also a more intense local irritation and bringing with it a greater proteolytic action.

Failure of a disinfection oleothorax is to be attributed to the nature of the lesion or faulty technic. The natural evolution of the disease in the pleura is often such that the oil is unable to inhibit the progress of the lesion, which may be in the lung cortex. In other cases the infected pleura is so thick that the oil is not permitted to exert its influence upon the deeper-lying infected structures. Failure, as a result of faulty technic, is usually due to the fact that

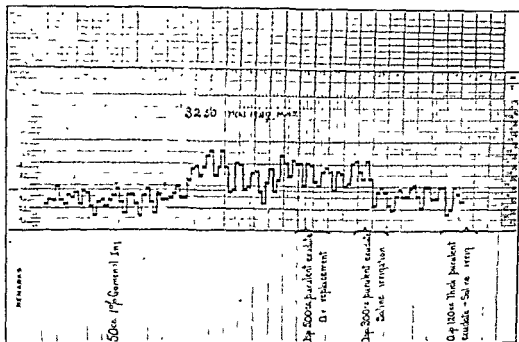


Fig. 19—Temperature curve in a case of mixed infection empyema following a lung perforation. The case was treated successfully by means of a disinfection oleothorax, after which a complete oil blockade was maintained for three years.

sufficient quantities of oil were not used in order to maintain an antiseptic bath of the entire serosa.

**Classification of Pneumothorax Empyemata.** — The pneumothorax empyemata are classified, for therapeutic purposes, into the nontoxic, or tolerable, and the so-called toxic, or virulent types. This classification serves from every standpoint much better than one based upon the bacterial flora of the empyema contents for the following reasons: In many cases, the causative organism cannot always be demonstrated; furthermore, the same organism provokes entirely different reactions under apparently similar conditions even in the same individual. And, lastly, the same anatomical changes can be produced by a wide variety of damaging agents, both bacterial and chemical.

The nontoxic, or tolerable, empyemata comprise those cases of pneumothorax empyema which pursue a torpid course, and are afebrile or subfebrile, intermit-

tently or permanently. These empyemata may be attended, in their beginning, with a very high fever, which might even lead one to suspect their virulent character. However, the fever usually falls after a few aspirations, the inflammatory process subsides and, aside from the reformation of a purulent exudate the patient suffers no inconvenience and exhibits no subjective phenomena.

In the nontoxic empyemata, a disinfection oleothorax is frequently attended by almost miraculous results, the empyema disappearing completely within the space of a few weeks. In other cases the reformation of the exudate persists, and it is therefore necessary to maintain an antiseptic-oil bath over a prolonged period of time.

The toxic, or virulent, pneumothorax empyemata are usually associated with a mixed infection. Their prognosis is unfavorable even from the very beginning. These cases are characterized by high fever of the hectic type, which may attain a daily maximum of 103° or 104° F. (Fig. 19). The patient is profoundly ill and toxic. There is complete anorexia, as a result of which the patient's strength is quickly exhausted. The patients, for the most part, are candidates for active surgical intervention, which usually begins with a pleurotomy and tube-drainage. If the patient survives, he is then a subject for a major surgical collapse. The disinfection oleothorax is a perfectly justifiable procedure in these cases; it cannot possibly do the patient harm and may spare him the necessity for surgical interference. As Kuss<sup>10</sup> points out, success can scarcely be expected unless the treatment is employed properly at the right time and not as a measure of last resort.

*Technic for Disinfection Oleothorax.*—The technic employed in a disinfection oleothorax depends upon the type of case at hand. The nontoxic, avirulent varieties usually require only aspiration of the purulent exudate, which is replaced with an equal volume of 5 per cent gomenolized paraffin oil. In the virulent forms it is extremely important to drain the pleural cavity completely of its purulent exudate, and irrigate thoroughly with normal saline solution until the return flow is clear, after which the exudate is replaced with an equal volume of 10 per cent. gomenolized paraffin, olive or Wesson oil.

Since irrigation is not required in the nonvirulent types of empyema, a 13 gauge needle, equipped with a one-way stopcock, is inserted into the lowermost portion of the pyothorax cavity, in the manner already described. The patient is next seated upright and inclined in the proper position to facilitate aspiration (Fig. 20). A 100-c.c. syringe is next connected with a four-way stopcock, and 100 c.c. of exudate are withdrawn. The stopcock on the arm leading to the chest is then closed and that on the lateral arm leading to the discard flask is opened. The syringe is then emptied of its contents and the valve closed. The valve on the other lateral arm is next opened and 100 c.c. of air are drawn into the syringe and injected into the pleural cavity, replacing the exudate withdrawn. This process of aspiration of exudate and air replacement is continued until one recovers pure, clear oil. The patient is next placed recumbent in the dorsolateral position and a quantity of oil equivalent to the amount of exudate removed is injected, replacing an equal quantity of air which is withdrawn. In this manner one avoids altering the intrapleural pressure too greatly

The oil injection and air replacement can be carried out in units of 100 c.c. in pyothorax cases, because more or less thickening of the pleura always exists and the patient is not as sensitive to changes in the intrapleural pressure as in the early phases of an inhibition or compression oleothorax.

After the injection of oil has been completed, a few drops of tincture of iodine should be allowed to flow through the needle track while the needle is being withdrawn, in order to prevent a needle-track infection.

The technic employed in the treatment of the virulent, toxic types of empyema varies little from that already described, except that, after aspiration

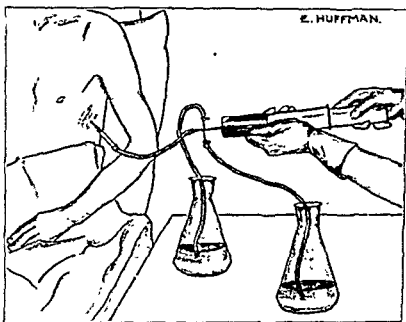


Fig. 20.—Illustrating method of irrigating pleural cavity. The needle is introduced into the most dependent portion of the empyema cavity. The syringe is equipped with a four-way stopcock. The exudate is aspirated and injected into container at left; container at right holds irrigation solution

of the purulent exudate, the pleural cavity must be thoroughly irrigated with saline solution until the return flow is absolutely clear. As much as 1000 to 10,000 c.c. of saline solution may be necessary. With that end in view, a 13 gauge needle is joined by means of a glass adapter and rubber tubing to a four-way stopcock, which is connected with a 100-c.c. syringe. The needle is inserted as already described, after which the patient assumes the sitting position, or is inclined in a manner to facilitate proper aspiration (Fig. 20). One hundred cubic centimeters of exudate are then aspirated and replaced with 100 c.c. of air. This maneuver is continued until the pleural cavity has been drained entirely of its contents. Irrigation is then accomplished as follows: 100 c.c. of saline solution are aspirated into the syringe, injected into the pleural cavity, withdrawn, and ejected into the discard utensil. This procedure is continued until the return flow is clear. This method of irrigation, while

effectively removing pus, nevertheless is not sufficient to wash the entire wall of the pleura. If a large amount of exudate has been present, it is therefore advisable to place the patient recumbent in the dorsolateral position, resting on the contralateral side, after which the pleural cavity is partially filled with warm saline solution, replacing an equal volume of air which is withdrawn. The patient is then seated upright and shaken so that the entire serosa is

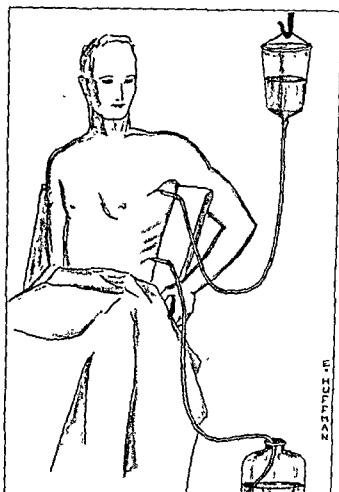


Fig. 21.—Method of continuous irrigation of pleural cavity in treatment of severe toxic types of pneumothorax empyemata.

washed. The irrigation solution is withdrawn and replaced with air. This method of irrigation is also continued until the return flow is clear.

In still other cases, it will be found that enormous quantities of saline solution or 1 per cent. Dakin's solution are necessary in order to effect a complete removal of the pus. We then frequently insert a second needle high in the axillary region, connecting it by means of rubber tubing with a glass irrigation container holding warm saline solution or Dakin's solution (Fig. 21). A thorough irrigation of the pleural cavity is then accomplished by permitting the solution to flow into the empyema cavity through the upper needle and out

through the lower one. If the discharge from the lower needle is not free, drainage can be facilitated by connecting it with a syringe and aspirating. The irrigation must be continued in this manner until the return flow is clear, and as high as 10,000 c.c. of irrigation solution may be required.

After the pleural cavity has been thoroughly irrigated, the patient is again placed recumbent in the dorsolateral position, after which the disinfecting oil, in a volume equal to the amount of exudate removed, is injected into the pleural cavity, replacing an equal amount of air. A few drops of iodine are allowed to flow into the needle track while the needle is being withdrawn. These methods of aspiration, irrigation and oil replacement are usually followed by an immediate fall of the fever, but they should be repeated as soon as the temperature again rises, and continued until the fever entirely disappears. These treatments may have to be applied every two or three days in the beginning, but, after the fever subsides, the intervals are lengthened to a week or more. Once the temperature reaches normal and remains there, irrigation is no longer necessary. The case is then treated according to the method described for the nontoxic types of empyema. In one of our cases, we were obliged to aspirate and irrigate 53 times during the course of 8 months, but the end-result was satisfactory, inasmuch as we succeeded in ridding our patient of a virulent empyema associated with intermittent pleuropulmonary fistula.

#### LATE COMPLICATIONS.

In addition to those reactions and complications occurring early in the course of oleothorax therapy, there are also late complications occurring at a time when the object of the oleothorax is being temporarily accomplished. We have used the term "late complications" to designate those changes which occur after the lapse of months or even one to two or more years, during which time the oleothorax has served its purpose.

In the case of an inhibition oleothorax, the collapse has been satisfactorily maintained, while in the case of a compression oleothorax the collapse has been reestablished, and, in that of a disinfection oleothorax, the empyema has been got rid of and a collapse has been maintained by means of an oil blockade of the pleural cavity.

Late complications are classified as follows: "intrapleural" and "extrapleural." The *intrapleural complication* consists of an exudate formation which may be serous, seropurulent or purulent. The exudate formation, particularly in the serous types, is not always associated with constitutional symptoms. On the other hand, the formation of a purulent exudate is usually accompanied or preceded by a gradually rising temperature. Many of these patients complain of a "cold" from which they have not recovered. However, a careful analysis of the symptoms will reveal that the patient did not become ill with any of the characteristic symptoms of an ordinary grippe, such as rhinitis, cough, expectoration, etc., and still more careful interrogation will elicit the fact that the patient only "felt like he had a cold." A study of the temperature record will show that there has been a gradual rise in temperature during the course of

several weeks, to, finally, a maximum of 100° F. or 101° F. daily (Fig. 22). Even then the unsuspecting patient will still claim that his condition is due to a "cold" from which he has not recovered.

In one of our cases a disinfection oleothorax has been carried out for the treatment of a tuberculous pneumothorax empyema. The empyema cleared up entirely, after which a complete oil blockade was established to combat an early obliterative pneumothorax. Fifteen months later, during which time the

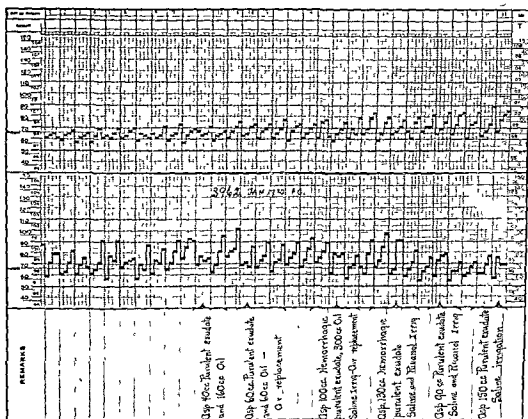


Fig. 22.—Temperature curve of patient developing a tuberculous empyema, after an oleothorax had been maintained for three years. The patient attributed the fever to a cold from which she had not recovered, even though respiratory symptoms were absent. Exploration of the pleural cavity revealed a purulent exudate containing tubercle bacilli. In this case a disinfection oleothorax, using 50 per cent. gomenolized paraffin oil, was originally instituted for the treatment of a tuberculous empyema. The exudate disappeared completely and remained absent for three years, during which time an inhibition oleothorax was maintained. The gomenolized oil did not prevent the occurrence of a complication which it had previously "apparently" relieved.

oil blockade remained uncomplicated, the patient was suddenly seized with "grippy" sensations (aches and chills), persistent nausea and vomiting. The temperature rose steadily, reaching 103° F. on the third day (Fig. 23). Symptoms referable to the chest were completely lacking and the patient attributed his condition to a so-called gastrointestinal "upset." However, an exploration of the oleothorax cavity revealed a purulent exudate. In this case we were con-





exudate in a pleural cavity already blockaded with oil may so elevate the intrapleural pressure that a lung perforation takes place.

Complications of this type, occurring late in the course of oleothorax therapy, are treated according to indications. In some cases the simple aspiration of the purulent exudate, until one recovers pure oil, suffices to bring about relief. This process of aspiration of purulent exudate until clear oil is recovered may have to be repeated several times, but one is not justified in abandoning the oleothorax immediately unless the condition fails to respond to a few aspirations. In one of our cases, after a complete oil blockade of the pleural cavity had been established, we were forced, during the course of fourteen months, to abandon the oleothorax on four different occasions because of the development of a purulent exudate associated with a high fever. On the fifth attempt we were able to reestablish a satisfactory oleothorax, which has now been maintained for more than four and a half years. I have in mind many other cases in which we were successful in permanently establishing an oleothorax only after several attempts. In two of our cases, the patients complained only of great prostration and weakness. The symptoms developed after a complete oil blockade of the pneumothorax cavity had been effected. In both cases the oleothorax was temporarily abandoned, after which the symptom complex completely subsided. In both cases the oleothorax was later reestablished and again abandoned because of the same condition.

The late *extrapleural complications* are of a visceral and parietal character.

**Visceral Character.**—Pleuropulmonary perforation is the only late complication of a visceral character to be contended with, and is serious. The perforation is usually preceded by a period of a few days, during which time the patient raises considerable quantities of a peculiar watery or mucous secretion. Unless the intrapleural pressure is immediately reduced, there soon follows the smelling of oil, then the tasting of oil, and finally the expectoration of oil. In other cases the perforation occurs suddenly without the patient previously complaining of any untoward symptoms.

While large perforations are permanent and require a thoracoplasty if recovery is to take place, small perforations frequently heal or assume an intermittent character. If the perforation is small, the oleothorax should be partially abandoned, at least half of the oil being replaced with air. But, if in spite of this treatment a leak persists, the oleothorax should be abandoned temporarily. Later on, the presence of the perforation can be determined by testing the permeability of the pleura. This is usually done by: (a) giving an air inflation and watching the behavior of the manometer; (b) permitting nitrogen gas to flow into the pneumothorax cavity—if a leak is still present, the patient will experience a metallic taste in the mouth; (c) injecting into the pleural cavity  $\frac{1}{2}$  c.c. of any aromatic oil, such as sandalwood oil or a few cubic centimeters of 1 per cent. gomenolized paraffin oil—if a leak persists, the patient will taste and smell the oil injected; (d) the permeability of the pleura can also be tested by injecting 10 to 20 c.c. of a 1 per cent. solution of methylene blue in saline solution into the pneumothorax cavity. The patient is then placed recumbent in the dorsolateral position, after which he is shifted about

so that the methylene blue solution flows over the entire visceral pleura. If a perforation is present, the dye will be shortly expectorated.

According to our experience, small perforations often heal completely. As soon as one is assured that healing has taken place, the oleothorax can be reestablished. While most patients experiencing a perforation of any proportion are relieved only by a thoracoplastic collapse, this is not always the case.

In his oleothorax work, Fontaine<sup>19</sup> reported 12.8 per cent. deaths from pleuropulmonary perforation. Bernou<sup>18</sup> reports that in ten years he has observed 16.1 per cent. perforations, 5.4 per cent. of which were fatal. Russell and Houriet<sup>20</sup> state that perforation occurs in from 12 to 14 per cent. of all cases wherein a large oleothorax has been established. Morin<sup>21</sup> in a series of 91 cases, observed perforation in 18, 20 per cent. In our own work, covering observations on our first 100 cases, pleuropulmonary perforation occurred in 17 cases, 17 per cent.—of this number, four patients are dead. In no instance could death be attributed to the perforation. In one case the patient died months after the perforation, as a result of the natural evolution of her disease. The other three cases died months after the perforation, as a result of a thoracoplasty performed elsewhere. Two cases recovered after a thoracoplastic collapse. Five cases received a pleurotomy with tube drainage. Four of these cases will require a thoracoplastic collapse if recovery is to take place. Of the remaining six cases, 5 are clinically well, the perforation having healed and the lung having fully expanded and attached itself to the chest wall. In one case the oleothorax is still being maintained but the perforation has been healed for more than two years.

In three of our cases the patient expectorated voluminous quantities of oil and exudate from the pleural cavity, necessitating immediate abandonment of the oleothorax, and, while we at first felt that nothing except a thoracoplastic collapse could bring about recovery, we nevertheless attempted to effect healing of the perforation by keeping the pleural cavity well drained of its contents and maintaining a neutral pressure by means of frequently repeated aspirations. In all three cases a complete and permanent healing took place, and the lung in all three cases is now fully expanded and attached to the chest wall.

**Parietal Complications.**—These consist of pleurocutaneous fistulæ, threatened empyema necessitatis, and paraffinoma. *Pleurocutaneous fistulæ* occur as the result of needle-track infections following the aspiration of a purulent exudate. In the virulent mixed-infection empyemata, the infection of the needle-track may occur within twenty-four hours. In the ordinary pyothorax cases, it may not manifest itself for weeks or months, when, suddenly, many previously clean puncture sites break down and exude pus. This complication can best be avoided by injection of the needle track with iodine as one withdraws the aspirating needle. In cases in which pleurocutaneous fistulæ exist, the pyothorax cavity should be punctured for aspiration purposes at its most dependent portion in the axillary region, and an effort should be made to expand the lung posteriorly, for the reason that if the patient is

destined to receive a thoracoplastic collapse, or an "undecking operation," the fistulous openings will occupy a site favorable for the undecking operation and away from the field of operation, if a rib resection is resorted to.

*Empyema necessitatis*, or threatened *empyema necessitatis*, occurs as the result of the confluence of many infected puncture sites in the pleura. As a result of the destruction of larger or smaller areas of the pleura, the purulent exudate invades the subcutaneous tissues and appears as a bulging mass beneath the skin. Rupture through the skin frequently occurs through the small openings representing former puncture sites. This bulging mass which appears in the side may be painless or attended with considerable inflammatory reaction. If the opening into the pleural cavity is large, the bulging mass subsides when the patient assumes the recumbent position, lying on the contralateral side. If the patient is asked to cough, the area will be observed to bulge as a result of the temporarily increased intrapleural pressure.

*Paraffinomata* occur in cases in which the oleothorax has been maintained under pressure. In such cases, the oil leaks from the pleural cavity through the needle-puncture hole into the subcutaneous tissues and appears as a large indurated mass which is usually painless. *Paraffinomata* can be avoided by the use of smaller-gauged needles which should be directed through the pleura at an oblique angle. A leakage of oil into the subcutaneous tissues can also be combated by covering the puncture site, first, with a small pledget of sterile gauze, which is then covered with one or two pieces of rubber sponge (about one inch square and one-third inch thick). This dressing is held firmly in position by strips of adhesive tape which are applied tightly to the chest.

#### END-RESULTS.

Satisfactory results can be expected in approximately 60 per cent. of the cases wherein the oleothorax has been employed for disinfection purposes—that is, the empyema clears up and the collapse can be maintained either by air inflations or a complete oil blockade.

When an oleothorax is employed to inhibit expansion, to reestablish collapse, satisfactory results can be expected in approximately 50 per cent. of the cases. By far the best results will be obtained in the elective oleothorax cases. The most unsatisfactory results will be obtained in cases wherein a compression oleothorax has been established.

Statistics concerning end-results are of little value unless the series is rather large and the period of observation is sufficient to warrant reliable conclusions. Unfortunately, with few exceptions, the statistics already published concern but a few cases (two to twenty) covering a very brief interval which is entirely inadequate to justify reliable conclusions. Our figures are based upon the end results of our first 100 cases and cover a period extending over nine years. Our results coincide very closely with those of other observers having had extensive experience, particularly Fontaine<sup>22</sup> on the basis of 100 cases, and Julian Marie<sup>23</sup> in a review of 50 cases.

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## CHAPTER XXII.

### PHRENIC NEURECTOMY.\*

RALPH C. MATSON.

After intrapleural pneumolysis has been utilized to its fullest extent as an adjunct to artificial pneumothorax, there will be a large group of cases with adhesions of a type not suited for operation; still an additional outstanding group will remain wherein pneumothorax is attempted but fails either because no gas can be introduced on account of pleuritic adhesions or the latter prevent the establishment of a pneumothorax of sufficient size or conformation to be of therapeutic value. Instead of continuing the useless pneumothorax, or subjecting the patient to further routine sanatorium care with perhaps a discouraging outlook and hoping it eventually will bring about a satisfactory clinical end-result, it is much better to consider the use of some other operative collapse measure. Before subjecting the patient to the more radical surgical procedures, such as extrapleural pneumolysis with fills, or direct cavity drainage, or thoracoplasty, one's next thought should be the possibility of phrenic neurectomy providing sufficient functional rest or collapse of the lung to promote healing.

#### INDICATIONS.

Operative procedures on the phrenic nerve are indicated under a wide variety of conditions, both in the tuberculous and nontuberculous diseases of the lung. In the nontuberculous pulmonary suppurations, excellent results have been observed in lung abscess and bronchiectasis. We have induced bilateral hemidiaphragmatic paralysis in bilateral bronchiectasis with extremely favorable results. In the tuberculous diseases of the lung, operative procedures on the phrenic nerve are indicated under the following conditions:

1. As an independent procedure in (a) all cases wherein an artificial pneumothorax is indicated and wherein adhesions have prevented introduction of gas, or wherein adhesions of an inoperable type prevent the establishment of a satisfactory collapse; (b) for social or economic reasons in cases wherein the patient is unable to undergo a prescribed course of pneumothorax therapy.

2. Before every thoracoplasty for the following reasons:

- (a) The improvement after an induced hemidiaphragmatic paralysis has been effected may lead to recovery—thus sparing the patient the necessity of a major surgical operation.

- (b) In favorable cases, the patient is rendered a far better surgical risk because of the marked improvement which often follows a satisfactory hemidiaphragmatic paralysis.

\*The cases upon which these observations are based include cases from the service of our associate, Dr. Marr Bissell, who has rendered much valuable assistance.

(c) Not only is the sputum quantity reduced but the cough is mitigated,—in this way the danger of aspiration infection (should a thoracoplasty be resorted to) will be reduced.

(d) To affect as much collapse as possible through the rising diaphragm, thereby reducing the number of ribs and amount later to be removed.

(e) To permit the heart to partially accommodate itself to the increased functional activity later to be imposed upon it by a thoracoplasty.

(f) As a test of the integrity of the contralateral lung.

According to some surgeons, the chief value of a phrenic neurectomy is as a "test" operation before a thoracoplasty in cases with suspicious changes in the better lung, particularly apical lesions. If the operation is followed by an increase of the physical or roentgenological findings, fever, or the patient's general condition becomes worse, an extrapleural thoracoplasty is absolutely contraindicated. On the other hand, if there is no reaction, one may safely proceed with the major operation.

A study of our material indicates that one cannot accept with blind faith the result of a phrenic neurectomy as a "test" operation, for we have seen a contralateral lung lesion withstand the "test" operation, but exhibit activity following a thoracoplasty. We have also observed an essentially negative contralateral lung exhibit disease following the "test" operation, but pass through a complete thoracoplasty undamaged, although the diseased area was essentially the same before each procedure.

3. Supplementary to artificial pneumothorax where nonseparable adhesions are preventing a satisfactory collapse—to provide additional collapse.

4. Threatened early obliterative pneumothorax combined with oleothorax to maintain collapse.

5. Towards the end of a course of pneumothorax therapy when one has had to deal with a lung originally having very extensive disease, in order to diminish the capacity of the hemithorax to accommodate a lung which has been shrunken by scar tissue changes, thus lessening the danger of (a) reëxpansion of excavated areas, (b) secondary bronchiectasis, (c) retraction of heart and mediastinal contents.

6. Following a course of pneumothorax therapy wherein the treatment has not been continued long enough to insure complete healing of the diseased process—to reëstablish collapse.

7. Empyema complicating pneumothorax, for the purpose of lessening the area of suppurative pleuritis.

Section of the phrenic nerve to artificially paralyze the hemidiaphragm was first proposed by Stuert<sup>1</sup> in 1911 for the treatment of severe unilateral tuberculosis of the lower lobe of the lung. Sauerbruch,<sup>2</sup> however, first performed the operation in 1904, in order to facilitate resection of the esophagus in the course of his animal experiments; he advocated the operation for those types of pulmonary tuberculosis wherein pneumothorax was indicated but its application prevented because of pleuritic adhesions hindering gas introduction. Sauerbruch's belief that rest and collapse of the diseased parts would favor healing

was supported by Schepelmann<sup>3</sup> in 1913, who stated that as a result of animal experimentation hemidiaphragm paralysis would favor healing of apical tuberculosis.

### OPERATIVE PROCEDURES.

The Stuertz operation consisted in exposing and cutting out a short section of the phrenic nerve at a point in the neck where it passes over the anterior surface of the scalenus anticus muscle. It has been shown that as a result of the procedure, one frequently obtains a collapse of the lung amounting to from one-fourth to one-third its volume: to a certain extent, then, the anatomical and physiological changes associated with a pneumothorax occur. Stuertz proposed resection of a short piece (a few centimeters) of the nerve to prevent its regeneration, but, in spite of this, the hemidiaphragm paralysis was either not complete or not permanent in many cases.

Bardenhuer<sup>4</sup> is recorded as having been the first to report this operation in 1912, although Oehlecker<sup>5</sup> published the reports of three cases in 1913, the first of which had been operated upon in 1911. In 1913, Sauerbruch,<sup>6</sup> without knowledge of Stuertz having proposed this operation, published a report of five cases.

At the eleventh annual meeting of the National Tuberculosis Association, Ralph C. Matson, in collaboration with Marr Bissailon,<sup>7</sup> reported two cases operated upon in 1914. They remarked that the operation was of doubtful value, as they had observed return of function in one case. During the next few years, in a small series of cases, they observed that the hemidiaphragm paralysis was not permanent in a large proportion of them, for which reason they abandoned the procedure.

Up to 1914, twenty-six cases had been operated upon by Sauerbruch in his Zurich Clinic. All were studied roentgenologically by Walther<sup>8</sup> who discovered that only five cases showed a permanent hemidiaphragm paralysis and that less than 50 per cent. exhibited the characteristic paradoxical movement.

Other operators reported that the *hemidiaphragm paralysis* was not permanent in a large proportion of cases, and the operation was generally discarded, until 1922 when Felix<sup>9</sup> and Goetze<sup>10,11</sup> showed that simple resection of the nerve as proposed by Stuertz was not sufficient because in fully 25 per cent. to 35 per cent. of all cases, the phrenic nerve, while taking its origin usually from the fourth and at times from the third and fifth—or all three cervical roots, also may receive additional fibers from the second, sixth, seventh and eighth and even the first thoracic. These accessory fibers join the phrenic below the site of resection proposed by Stuertz, and, therefore, continue to enervate the diaphragm in spite of simple phrenic neurectomy. Felix found an accessory phrenic nerve arising usually from the fifth cervical root in 25 per cent. to 35 per cent. of all persons. This accessory branch arises either near or with the subclavius nerve and then separates from it just before the latter enters the subclavius muscle, the accessory branch then continues downward in front of the subclavian vein to join the phrenic directly behind the sternal end of the first rib.

**Exaíresis of the Phrenic Nerve.**—In order to interrupt impulses coming from the accessory branches, as well as any communicating cervical sympathetic



fibers of the phrenic nerve, Felix proposed an exaïresis of the phrenic nerve after cutting it; this was accomplished by winding it around a Thiersch, or hemostatic forceps; the entire nerve may sometimes be extracted by the method. If 12 cm. of the nerve is evulsed, one may be certain that complete interruption of the phrenic and associate fibers has taken place. We have never seen a failure even when shorter sections (8 to 10 cm.) have been drawn out.

Goetze<sup>10,11</sup> objected to the *phrenicus exaïresis* of Felix, believing that there was danger of damaging important vascular structures or tearing into important structures in the mediastinum. As a means of surmounting these objections, he proposed resecting a small section of the phrenic nerve, then overcoming accessory impulses by resecting a small section of the nerve to the subclavius, as well as all accessory fibers between the phrenic and the cervical nerves.

In order to determine the merits of the operation proposed by Felix as compared with that of Goetze, Andreas Plenck, assistant in the surgical division of the Jubilæumspital, Vienna, and Ralph C. Matson<sup>12</sup> dissected out 112 phrenic nerves in cadavers. They found 72 per cent. typical phrenic nerves,—that is to say, the nerve arose from fibers of either the third, fourth or fifth cervical nerves which joined together in one main trunk and passed down across the anterior surface of the scalenus anticus muscle, entering the thorax behind the subclavian vein.

In thirty-two instances (28 per cent.) the formation of the nerve was atypical. Double phrenics with associate fibers on the face of the scalenus anticus were encountered eight times. In four instances, the associate phrenic came from the subclavius nerve. In one instance there was a bilateral, and in another a unilateral absence of a typical phrenic; there was no main trunk on the anterior surface of the scalenus anticus, but two large trunks emerged mostly from the fifth cervical close to the point of origin of the subclavius nerve. They ought really to be called "associate phrenics," as all three passed down in front of the subclavian vein. These latter three nerves came off so far lateralwards that they could not be located by the technic of Felix, nor by the usual surgical approach for a phrenic neurectomy.

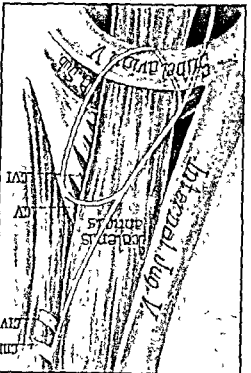
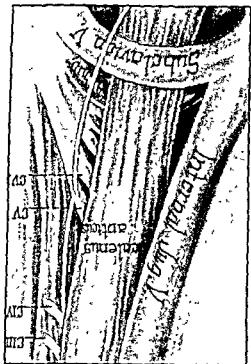
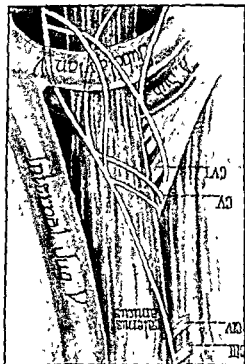
In all probability, the case encountered by Sauerbruch was one like the above mentioned, when location of the phrenic nerve proved a failure.

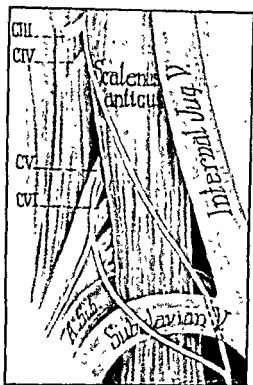
We have met with two such cases in our practice; the phrenic nerve could not be located on the anterior surface of the scalenus anticus, but it was found joined with the subclavius nerve. In both instances, resection of the nerve produced a perfect hemidiaphragm paralysis.

In twenty-three instances (Plates I, II, III and IV), the accessory phrenic fibers and subclavius nerve had a common origin from the fifth cervical. In six instances, the accessory phrenic arose apart from the subclavius nerve as a separate branch. In five instances, it formed a loop around the vein. In one instance, two associate phrenic trunks passed in front of the subclavian vein, then looped around behind the internal mammary artery.

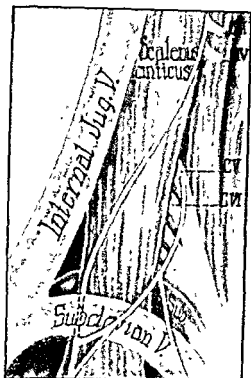
From these studies, it would seem that in case of a typical phrenic nerve, the exaïresis of Felix is adaptable, but even then, not without possible danger.

Plate I.—(a) Phrenic from *civ* with associate phrenic from *cv* passing behind subclavian vein and joining main stem of phrenic. (b) Phrenic arising from *civ* and *cv* with associate phrenic looping around the subclavian vein and joining main stem of the scalenus anticus. A dangerous type for excision. (c) Phrenic from *civ* and *cv*. Associate phrenic arising from the subclavian vein. A dangerous type for excision. (d) Dislocated phrenic arising from *civ* and *cv* passing in front of the subclavian vein. No main stem on surface of scalenus anticus. Not accessible by usual surgical approach.

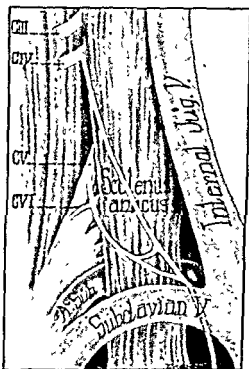




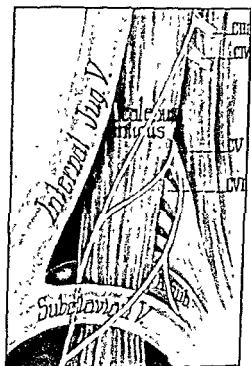
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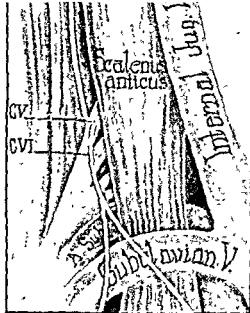


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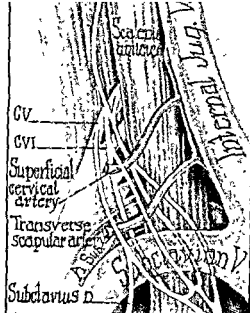


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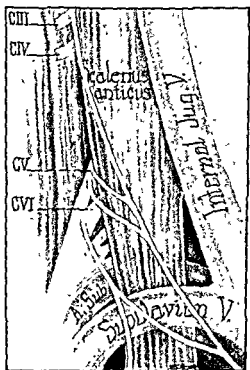
Plate II.—(a) Phrenic arising from *ciii* and associate phrenic from *n. subclavius* passing in front of the subclavian vein. (b) Phrenic from *ciii* and associate phrenic from *n. subclavius* bifurcating and both branches joining the main stem below the subclavian vein. (c) Phrenic arising from *ctv* with associate branch from *cv*. (d) Phrenic from *ciii* and *cv* with associate phrenic from *n. subclavius* passing in front of the subclavian vein.



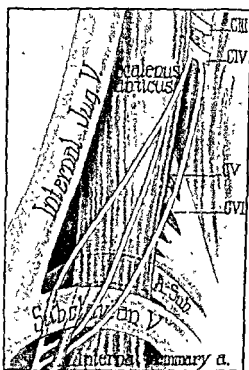
a



b



c



d

Plate III.—(a) Dislocated phrenic from *ciii* and *cv* arising with *n.* subclavius separating from it and passing in front of the subclavian vein. No main stem on the anterior surface of the scalenus anticus. Not accessible by usual surgical approach. (b) A very complex type of phrenic from *civ* and *cv* with four main stems, one of which passes in front of the superficial cervical and transverse scapular arteries and subclavian vein. A dangerous type for exaeresis. (c) Phrenic from *ciii* and *cv* with two associate branches, one from *cv* lateralward which joins the main stem of the phrenic on the anterior surface of the scalenus anticus, and the other associate branch arising from *cv* in common with the *n.* to the subclavius muscle. (d) Phrenic from *civ*. Two branches pass in front of the subclavian vein and behind the internal mammary artery. A dangerous type for exaeresis.